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Handbook of Pediatric Urology

Third Edition

Laurence S. Baskin
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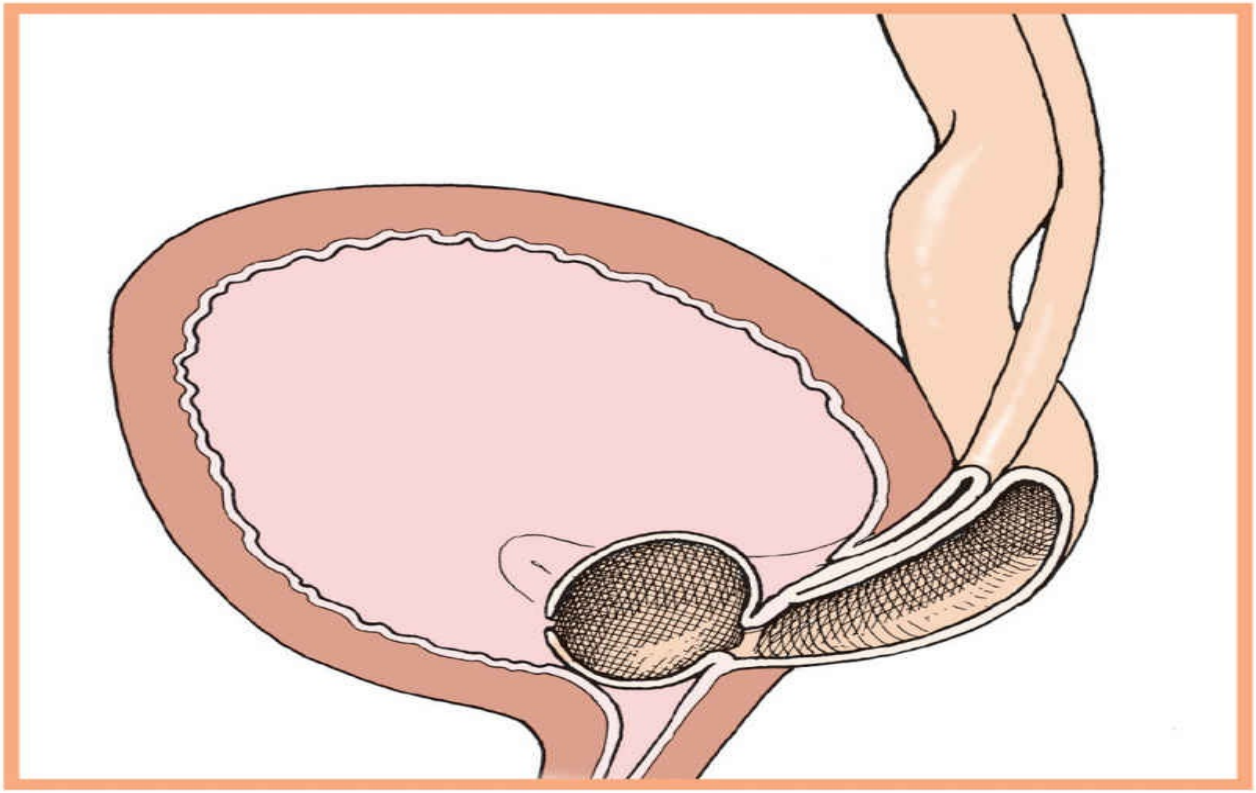
Jeffrey A. Stock



Wolters Kluwer

THIRD EDITION

Handbook of
Pediatric Urology

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We all have heroes that we look to for guidance and help. Mine was Dr. John Duckett, Jr., senior editor of this first edition of the *Handbook of Pediatric Urology*. Dr. Duckett was my role model and teacher for pediatric urology. He taught me the intricacies of patient care and the nuances of pediatric urologic surgery. Most importantly, his vibrant personality was reflected in the hope and spirit that he was able to give to his patients and colleagues. Dr. Duckett is greatly missed by all. The *Handbook of Pediatric Urology* is dedicated to his memory. His spirit lives on in all who have learned from this great teacher, leader, mentor, and friend.

Laurence S. Baskin, MD

PREFACE

A picture is worth a thousand words. Extensively illustrated for the benefit of patients, medical and nursing students, and health care professionals, the third edition of the *Handbook of Pediatric Urology* is a comprehensive resource to answer your pediatric urology questions. The handbook is an excellent complement for your office, clinic, emergency room, classroom, or white coat as you make hospital rounds. The chapters on the classic pediatric urology problems such as hypospadias, hydronephrosis, reflux, disorders of sex development, urinary tract infection, undescended testes, hernia and hydroceles, congenital anomalies and all other areas of pediatric urology have all been updated. In addition, the third edition has been expanded to include new chapters on robotics in pediatric urology, pediatric and adolescent gynecology, and sexually transmitted diseases in adolescence. Finally, the online version includes practice cases in multiple choice format with explanations to each case scenario.

We hope you find the third edition of the *Handbook of Pediatric Urology* an excellent resource.

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CONTENTS

1 Circumcision
Laurence S. Baskin and Karla M. Giramonti

2 Hypospadias
Laurence S. Baskin

3 Undescended Testes—Cryptorchidism
Guy A. Bogaert

4 Abnormalities of Sex Differentiation
Jason M. Wilson

5 Hydrocele, Hernia, Neonatal Torsion, and Scrotal Masses
Barry A. Kogan

6 Urinary Tract Infections in Children
Hillary L. Copp, Angelique M. Champeau, and Nicholas M. Holmes

7 Vesicoureteral Reflux
Hillary L. Copp and Laurence S. Baskin

8 Daytime Urinary Incontinence/Bladder and Bowel Dysfunction (in the Otherwise Healthy Child)
Angelique M. Champeau

9 Nocturnal Enuresis
Anne M. Arnhym

10 Constipation and Urologic Conditions
Angelique M. Champeau and Karla M. Giramonti

11 Spina Bifida/Neurogenic Bladder
Ronald S. Sutherland

12 Prenatal Urologic Diagnosis and Maternal Counseling
Barry A. Kogan

13 Neonatal Hydronephrosis
Barry A. Kogan

14 Hydroureteronephrosis: Ureteroceles, Duplications, Ureteral Ectopy
Laurence S. Baskin

15 Posterior Urethral Valves
Laurence S. Baskin

16 Congenital Anomalies: Urachal Anomalies, Exstrophy-Epispadias Complex, Imperforate Anus, Cloaca, and Prune Belly Syndrome
Joseph Borer

17 Adolescent Urology: Acute Scrotum, Varicoceles, and Delayed Puberty
Bruce J. Schlomer

18 Genitourinary Trauma and Priapism
Hubert S. Swana and James M. Betts

19 Hematuria
Kara N. Saperston

20 Nephrolithiasis in Children: Medical Management
Gregory E. Tasian

21 Urolithiasis in Children: Surgical Management
Hubert S. Swana

22 Acute Kidney Injury
Paul R. Brakeman

23 Chronic Kidney Disease
Paul R. Brakeman

24 Pediatric Renal Transplantation
Gerald C. Mingin and Jeffrey A. Stock

25 Pediatric Urologic Oncology
Michael Ritchey

26 Robotic and Laparoscopic Surgery in Pediatric Urology
Eric A. Kurzrock

27 Anesthesia for Pediatric Urologic Procedures
Melissa A. Ehlers and Igor Galay

28 Sports Recommendations for Children with a Solitary Kidney or Other Genitourinary Abnormalities
Jack S. Elder

29 Pediatric Urology and Child Sexual Abuse
Angelique M. Champeau

30 Pediatric and Adolescent Gynecology
Bruce J. Schlomer

31 Adolescent Urology: Sexually Transmitted Infections
Bruce J. Schlomer

32 Transitional Urology
Robert Caleb Kovell and Dana A. Weiss

33 Pediatric Urology Database
Jeffrey A. Stock

34 Online Pediatric Urology Recommendations
Laurence S. Baskin and Jeffrey A. Stock

Index

1 Circumcision

Laurence S. Baskin and Karla M. Giramonti

I. THE ORIGINS OF CIRCUMCISION

A. Egyptian artifacts date circumcision to 6,000 years ago.
B. Four thousand years ago the Old Testament references ritual circumcisions to be performed on the eighth day of birth with a flint knife.
C. Both the Old and New Testaments make numerous references to circumcision without any relationship to health benefits.
D. Widespread practice of circumcision originated in the 19th century, allegedly as a prophylaxis against disease.
E. The present incidence of circumcision in the United States is estimated to be between 30% and 90% of newborn males with a much lower incidence in Europe. Geographic variations exist, with the Midwest having a greater incidence of circumcision compared to the East and West coasts.
F. Circumcision is the most common operation performed in the United States.

II. AMERICAN ACADEMY OF PEDIATRICS RECOMMENDATIONS

In 1975 and 1983, the American Academy of Pediatrics stated that “there is no absolute medical indication for circumcision in the neonatal period.” This was revised in 2012 and the outcome leaned toward the benefits of circumcision stating, “Evaluation of current evidence indicates that the health benefits of newborn male circumcision outweigh the risks and

that the procedure's benefits justify access to this procedure for families who choose it." Those benefits included prevention of urinary tract infections, penile cancer, and transmission of some sexually transmitted infections, including HIV.

When circumcision is being considered, the benefits and risks should be explained to the parents and informed consent obtained.

III. POTENTIAL MEDICAL ADVANTAGES OF CIRCUMCISION

A. Prevent phimosis.
B. Repair phimosis.
C. Prevent balanoposthitis (superficial infection of the glans penis [balano] and foreskin [posthitis]).
D. Eliminate the risk of penile cancer.
E. May decrease the incidence of some sexually transmitted diseases (HPV and HIV), and thereby cervical cancer.
F. Reduces the incidence of urinary tract infection in neonatal males (newborns to 12 months of age) by approximately 10 fold.

IV. DISADVANTAGES OF CIRCUMCISION

A. Transient behavioral and physiologic changes that the infant experiences.
B. Pain.
C. Potential complications of circumcision.
D. Irreversible removal of the prepuce.

V. CONTRAINDICATIONS TO CIRCUMCISION

All males born with penile anomalies (hypospadias, epispadias, megalourethra).

VI. RELATIVE CONTRAINDICATIONS TO CIRCUMCISION

A. Bleeding diathesis.
B. Prematurity.
C. Severe medical problems.

VII. OTHER FACTORS

A. Emotional.
B. Cultural.
C. Religious.
D. Father's foreskin status.

VIII. NORMAL FORESKIN

A. **Development**
    1. The foreskin begins to develop in the third month of intrauterine life with normal completion by 4 to 4½ months.
    2. It is normal for the newborn's foreskin to be adhered to the glans.
    3. Separation of the foreskin from the glans penis occurs late in gestation with only 4% of newborn males having a completely retractable foreskin. In 50% of newborn males, the foreskin cannot be retracted far enough to visualize the urethral meatus.
    4. By the age of 6 months, 20% of boys have a completely retractable foreskin, and by the age of 3 years that number increases to 90%. By the teenage years, complete separation of the foreskin occurs in virtually all males.
B. **Foreskin Care**
    1. The uncircumcised penis needs no special care other than the same attention given to the rest of the body.
    2. Genital hygiene in little boys does not require retraction of the foreskin.
    3. For undetermined reasons, possibly folklore or tradition, many physicians, parents, and grandparents remain convinced that the foreskin must be retracted at an early age.

4. Painful early foreskin manipulation can lead to bleeding, scarring, phimosis, and psychological trauma for the child and parent.

IX. PHIMOSIS, PENILE ADHESIONS, AND PARAPHIMOSIS

A. Phimosis is defined as a narrowing of the opening of the prepuce, preventing it from being drawn back over the glans penis (typically from scarring and/or recurrent infection). Treatment in severe cases is by surgical release of the scarred tissue, which may be referred to as a cicatrix. In less severe cases, the phimosis will respond to local treatment with topical steroids. Betamethosone 0.05% ointment applied to the tip of the penis at the area of the phimosis for 6 to 8 weeks twice a day has a 50% to 90% success rate. After one week the patient or parent should gently stretch the foreskin to facilitate release of the phimosis.

B. Penile adhesions in children with and without circumcision will typically resolve over time without the need for formal treatment. If concerning to parents they may also be treated with topical steroids in the same fashion as described for phimosis. Recalcitrant adhesions after circumcision may require surgical release. Simple adhesions can be lysed with the use of EMLA (eutectic mixture of local anesthetics) cream and a sharp iris scissors in the office. More dense adhesions or multiple adhesions may require general anesthesia.

C. Paraphimosis is defined as a painful constriction of the glans penis by the foreskin, which has been retracted behind the corona of the glans penis. Prolonged retraction of the foreskin leads to a relative obstruction of the lymphatics. This may cause lymphedema distally. Treatment requires reducing the foreskin after manual compression of the edematous glans penis. In severe cases, the constricting foreskin may need to be surgically released via a dorsal slit (see below).

X. METHODS OF CIRCUMCISION

The goal of circumcision is to remove an adequate amount of shaft skin along with inner-preputial skin so as to obtain an acceptable cosmetic result and prevent future development of phimosis and paraphimosis. There are four major techniques, which are described below.

A. **Dorsal Slit**

The dorsal slit is performed by incising the dorsal aspect of the foreskin, exposing the glans and thereby preventing phimosis and paraphimosis, but this alone is usually unacceptable from a cosmetic viewpoint. The dorsal slit is reserved for acute cases of phimosis or paraphimosis.

B. **Shield Technique (Mogen Clamp)**

The Shield technique requires separation of the adhesions between the foreskin and the glans (Fig. 1-1 A–C). The shield protects the glans by forcing it away from the stretched penis. The excess skin is excised and hemostasis secured by manual compression.

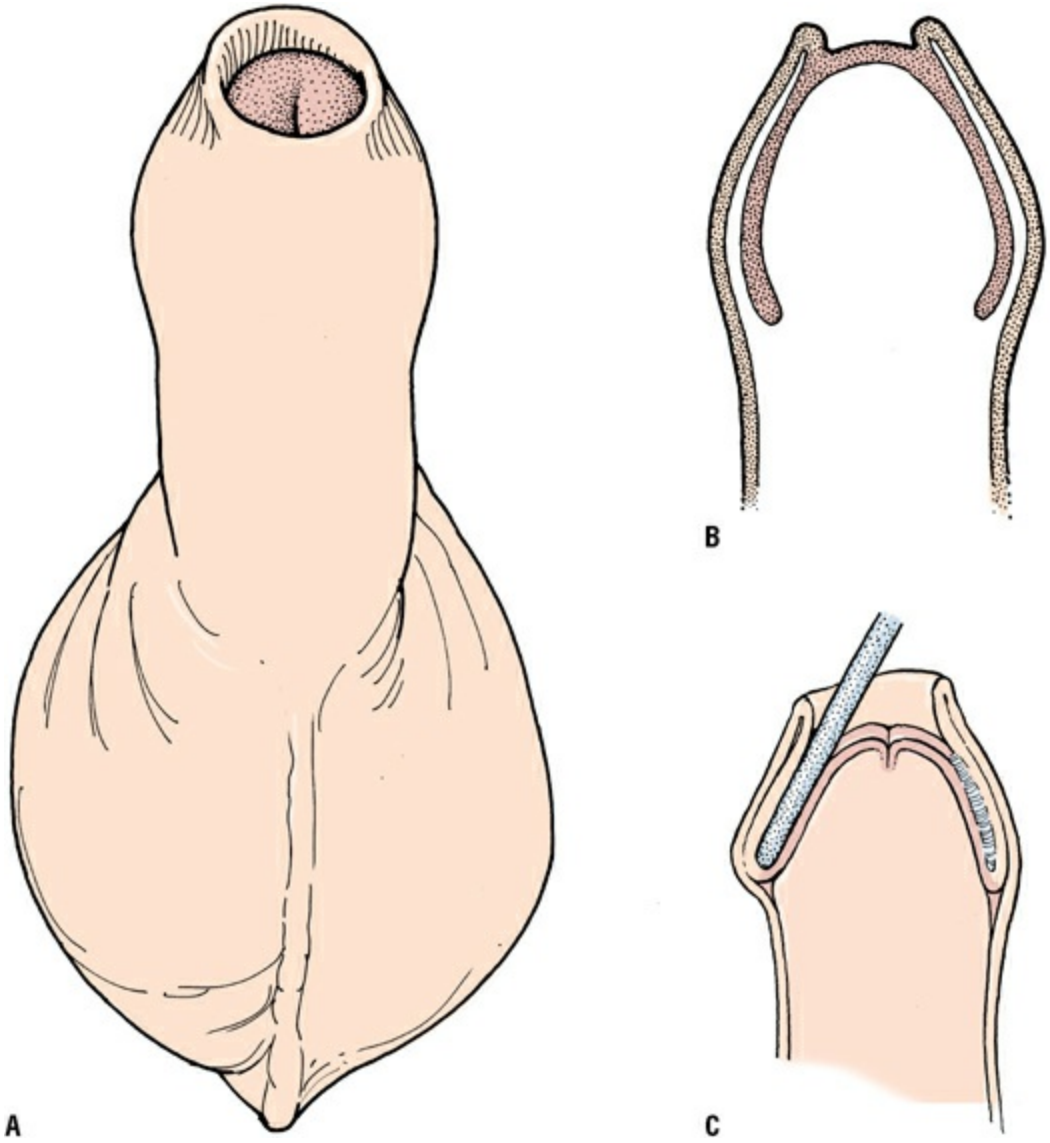

Fig. 1-1 A–C Schematic of separation of the prepuce from the glans, the critical step in a successful circumcision.

C. **Gomco Clamp (Fig. 1-2) or Plastibell Clamp (Modifications of the Shield Technique)**

When using a Gomco clamp, after freeing the inner preputial adhesions, the prepuce is drawn through a ring and hemostasis secured by pressure between the ring and the Gomco clamp. If any separation occurs between the opposed skin edges after removing the foreskin, the healing occurs by either secondary intention or primary suture. In the Plastibell technique, excess prepuce is allowed to necrose off (typically within 3 to 7 days) by

placing a tight suture across the excess foreskin. A more common practice is to cut the prepuce off just distal to the absorbable suture. In both the Gomco and the Plastibell techniques, the glans is protected by the respective clamps.

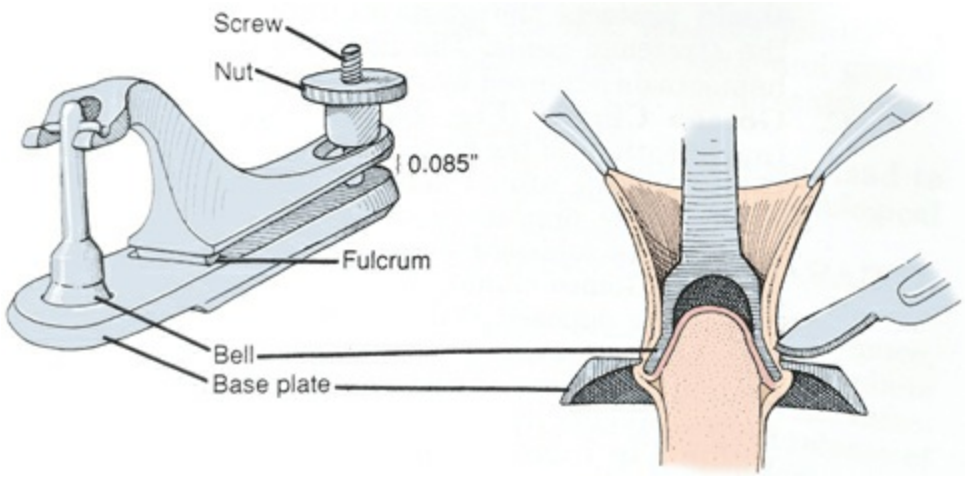

Fig. 1-2 Schematic of Gomco clamp and application to penis.

D. **Freehand Surgical Excision (Fig. 1-3 A–C)**

This is done by a combination dorsal slit or Sleeve technique and the wound is primarily closed by approximating the skin with small absorbable sutures.

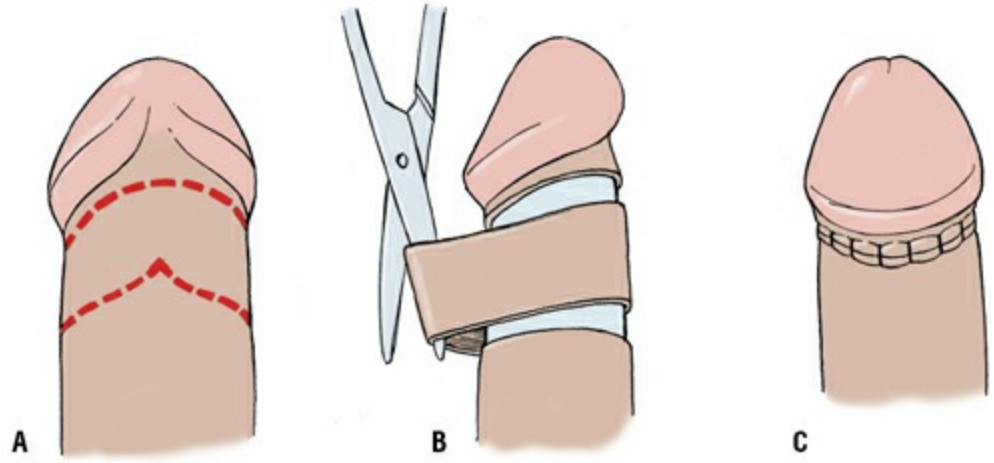

Fig. 1-3 A–C Schematic of freehand circumcision technique.

XI. COMPLICATIONS OF CIRCUMCISION

Most complications of circumcision can be avoided by careful

attention to complete separation of the glans from the inner preputial epithelium (Fig. 1-1 A–C), careful symmetric removal of the inner and outer preputial skin collar, and attention to hemostasis. Incidence of circumcision complications has been estimated to range from 0.2% to 5%. Complications are listed in Table 1-1.

A. **Acute**

1. Bleeding is probably the most common acute complication and it is typically controlled by direct pressure (the rare case will require placement of a suture).
2. Partial penile amputation (glans or corporal injury) is a very rare complication of circumcision. If an amputation injury occurs, the patient should be immediately transported to the care of a pediatric urologic surgeon for an attempt at immediate penile reconstruction (with the amputated part preserved in ice). Injury to the glans penis is typified by excess bleeding at the time of circumcision, or bleeding that is difficult to control with direct pressure.
3. Infections after circumcision are usually self-limiting and respond to local dressing changes. Serious necrotizing soft tissue infections have been reported, but are quite rare.
4. Skin issues: If during the course of routine circumcision an excessive amount of skin is inadvertently removed, such as the penile shaft skin, this should be treated by local wound care with a barrier cream such as Vaseline and the penile skin allowed to heal by secondary intention. Rarely, if ever, is immediate penile skin grafting necessary. More common is too little skin being removed in an asymmetric fashion; this can be treated electively. The use of electrocautery as a means for hemostasis during circumcision has been avoided because the current may be carried through the penile blood

supply, resulting in thrombosis and necrosis of the glans penis. With modern electrocautery equipment this should be extraordinarily rare.

B. **Non-acute**

1. Meatal stenosis is essentially unheard of in uncircumcised males and is most likely a result of meatitis and meatal ulcers, which presumably occur because the meatus is no longer protected by the prepuce. The mechanism of meatitis is most likely an irritant action of ammonia that is produced by bacteria in a urine-soaked diaper. The meatus may also be subjected to mechanical trauma from rubbing against the diaper. Diagnosis of meatal stenosis is not based on visual inspection of the urethral meatus, but on visualization of the urinary stream. If the stream is deviated significantly, usually greater than 30° in an upward direction, a functional impairment with respect to hitting the toilet with the urinary stream is present and a meatotomy is indicated. Meatotomy in an older cooperative child can be performed with the use of EMLA cream in the office. Younger children will require a brief general anesthetic.
2. Skin issues: Late complications that may require revision of circumcision include inadequate foreskin removal, asymmetric skin removal, skin bridges that occur from the raw surface of the glans healing to the cut edge of the foreskin, epidermal inclusion cysts that occur when an island of skin is left to heal underneath the skin, and penile curvature that can occur from skin tethering secondary to scar tissue from a circumcision that was performed at the time of acute inflammation.
3. Urethral cutaneous fistulas are a known complication secondary to aggressive removal of the foreskin with entrapment of the penile urethra and/or subsequent ischemia from a crush injury.

TABLE 1-1 Circumcision Complications

Acute	Non-acute
Bleeding	Skin loss
Infection	Skin excess
Amputation	Skin asymmetry
Urinary retention	Skin bridges
	Skin chordee
	Epidermal inclusion cyst
	Concealed penis
	Phimosis
	Meatal stenosis
	Urethrocutaneous fistula

XII. LOCAL ANESTHESIA FOR NEONATAL CIRCUMCISION

Techniques include the following.

A. **Dorsal Penile Nerve Block**
Lidocaine (0.2 to 0.4 cc of 1% lidocaine without epinephrine) is injected with a 27-gauge needle at the base of the penis at both the 10 o'clock and 2 o'clock positions dorsal laterally to infiltrate the neurovascular bundle.

B. **Circumferential Block at the Base of the Penis**
This is done with a 25 or 27 tuberculin syringe using 0.6 to 1.0 cc of 1% lidocaine (without epinephrine) at a single injection site ventrally at the penoscrotal junction. Care is taken to angle the needle laterally to avoid the urethra and a bilateral subcutaneous infiltration is achieved. The circumcision is performed 3 to 5 minutes after injection, allowing time for the anesthetic to take effect.

Both techniques have the potential complication of local hematoma and bleeding.

C. **EMLA Local Anesthetic Circumcision Technique**
EMLA stands for a eutectic mixture of local anesthetics which has not been approved for use in infants younger

than one month of age, or infants under the age of 12 months who are being treated with methemoglobin inducing agents. EMLA can be applied directly to the foreskin and has been useful as an anesthetic for meatal stenosis and may possibly have a role in pediatric circumcision.

D. **Oral Agents**
   1. Tylenol
   2. Sucrose
   3. Pacifier
   4. Manischewitz wine

XIII. POSTOPERATIVE CARE OF NEWBORN CIRCUMCISION

A. Proper postoperative care has the objective of minimizing postoperative bleeding, avoiding the formation of adhesions, skin bridges, buried penis, and preventing infection.
   1. Postoperative care begins with a proper bandage. Recommended is either a Vaseline or Xeroform bandage.
   2. An approximate 1- × 10-inch strip is cut from the prepackaged dressing and gently wrapped around the coronal sulcus.
   3. The bandage is left for 24 hours if it has not fallen off with the first diaper change, and KY or antibiotic ointment may be applied to the exposed penis and Vaseline to the diaper.
   4. If the Xeroform gauze has not fallen off in 24 hours, it is gently soaked off with cotton balls and tepid water. At that time the skin at the head of the penis is pushed back so the groove can be seen under the glans penis, that is, the coronal sulcus; this prevents penile adhesions. A wet Q-tip can aid in this process.
   5. Parents are counseled that a few drops of blood or ooze may be seen on the diaper. Typically the baby may bathe at the time that the umbilical cord has

fallen off. A soft yellow scab should not be confused with infection or pus. It is normally present and will fall off in time and should not be removed.

B. The major complication that occurs and can be prevented at a 1-week follow-up visit is adhesions of the mucosal skin to the glans penis.

   This can be corrected at this one-week visit by gently pushing the skin at the head of the penis back so the groove under the glans penis is visible thereby breaking up any adhesions that have formed.

RECOMMENDED READING

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2 Hypospadias

Laurence S. Baskin

I. INTRODUCTION

A. Hypospadias is a congenital defect of the penis, resulting in incomplete development of the anterior urethra, corpora spongiosum, and prepuce (foreskin).
B. Clinically, the hypospadiac urethral meatus does not cause significant symptoms other than a urinary stream that may be deflected in a downward fashion.
C. Hypospadias is also associated with penile curvature and in severe cases may result in infertility secondary to difficulty in semen delivery or associated abnormalities in testicular function.
D. Hypospadias is not associated with an increased risk of urinary tract infection.
E. Severe hypospadias with or without associated cryptorchidism should be evaluated for a Disorder of Sex Development (Chapter 4).

II. EMBRYOLOGY

A. At 2 months gestation the male and female genitalia are essentially indistinguishable.
B. Under the influence of androgens, the male external genitalia become masculinized.
C. By the end of the first trimester, approximately 17 to 18 weeks, the penile urethra and accompanying prepuce are completely formed.
D. Abnormalities in this development can lead to hypospadias and associated penile anomalies.

E. In hypospadias, incomplete development of the glandular urethra does not allow the preputial folds to fuse.

F. Consequently, in hypospadias the foreskin is absent on the ventrum and there is excessive foreskin on the dorsal surface (dorsal preputial hood).

III. CLASSIFICATION

A. Hypospadias can be classified as mild, moderate, or severe based on the location of the ectopic urethral meatus along the ventral aspect of the glans or coronal (mild), penile shaft (moderate), or penoscrotal junction, scrotum, or perineum (severe). It is important to take into account associated penile curvature, which will increase the complexity of hypospadias and hence surgical repair.

B. A more useful surgical classification is the location of the meatus after penile straightening or chordee correction at the time of reconstructive surgery.

1. Fifty-five percent of the patients will have anterior hypospadias with the meatus on the glans or subcoronal (Fig. 2-1 A).
2. Thirty percent will have the urethral meatus on the penile shaft (Fig. 2-1 B).
3. Fifteen percent will have the meatus between the perineum and the penoscrotal junction (Fig. 2-1 C).

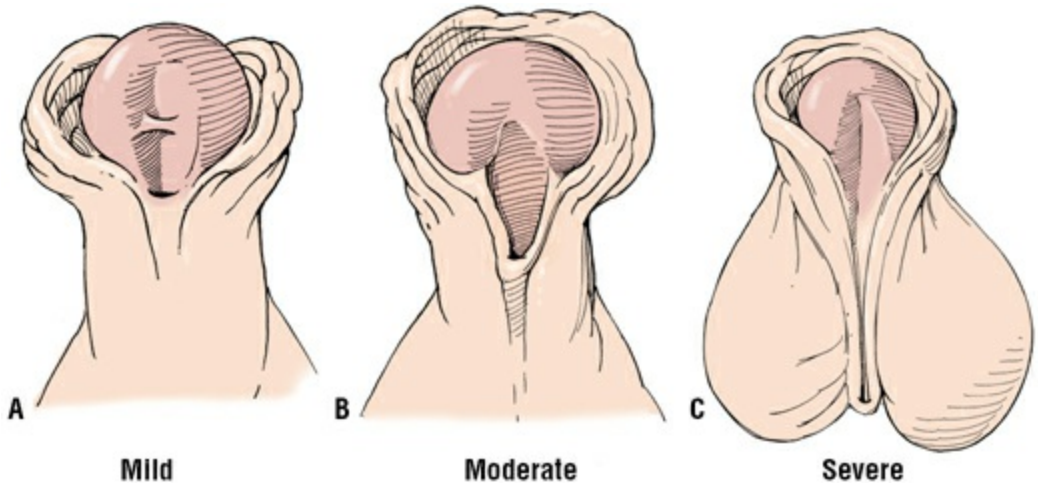

Fig. 2-1 Classification of hypospadias. A: Anterior hypospadias. B: Penile shaft hypospadias. C: Scrotal hypospadias.

C. A rare form of hypospadias occurs in less than 1% of patients where the foreskin is circumferential and the ectopic meatus is discovered when taking down the physiologic foreskin adhesions at the time of circumcision. These patients have a wide meatus located near the coronal margin, the so-called megameatus intact prepuce. This can be successfully repaired with and without preservation of the foreskin.

IV. INCIDENCE, GENETICS, AND ETIOLOGY

A. Hypospadias occurs in 1 per 250 live male births.
B. There is a 14% incidence in male siblings and an 8% incidence in offspring of patients with hypospadias.
C. The majority of cases of hypospadias have no known etiology. Extensive research into abnormal androgen metabolism or the levels of the androgen precursors, testosterone and the more potent dihydrotestosterone, has revealed only a small percentage of patients with any abnormalities. A classic example would be the rare patient with 5α-reductase deficiency and associated severe hypospadias.
D. Environmental pollutants or endocrine disruptors have been suggested to cause hypospadias by maternal exposure that is carried to the developing fetus. Case report human data and experimental animal data are cause for concern and further investigation is warranted.

V. ASSOCIATED ANOMALIES

A. Undescended testes occur in approximately 9% of patients with hypospadias.
B. There is an increased incidence of up to 30% in patients with penoscrotal or more severe hypospadias.
C. Inguinal hernias also occur in approximately 9% of patients with hypospadias.
D. A prostatic utricle or müllerian remnant in the posterior urethra is found in a high percentage of patients with

severe hypospadias. Prostatic utricles in hypospadias are typically of no clinical consequence but can make catheterization difficult.

E. Associated urinary tract anomalies are infrequent in patients with isolated hypospadias because the external genitalia are formed embryologically much than the kidneys, ureter, and bladder.

F. Patients with mild hypospadias and an undescended testicle or an inguinal hernia do not need further urinary tract evaluation.

G. Patients who have hypospadias in association with other organ system anomalies such as a cardiac murmur, imperforate anus, limb malformations, cleft lip, or pyloric stenosis require renal and bladder imaging with an abdominal ultrasound.

H. As noted, patients with severe hypospadias with or without undescended testes should be investigated for a disorder of sex development with a karyotype and further endocrinologic workup (see Chapter 4). Basic testing includes karyotype, serum testosterone and dihydrotestosterone, and a pelvic sonogram.

VI. TREATMENT OF HYPOSPADIAS

A. There are five basic principles for the successful reconstruction of the hypospadiac penis.
   1. Creation of a normal urethral meatus and glans penis.
   2. A straight penis.
   3. A normal urethra.
   4. Skin covering.
   5. Normal position of the scrotum in relationship to the penis.

VII. TIMING OF SURGERY

A. Hypospadias surgery is best performed between the ages of 6 months and 18 months, prior to toilet training and during the psychological window when genital awareness

has not been recognized by the patient.

B. Outpatient surgery is now the standard of care. The majority of hypospadiac defects can be repaired in a single-stage operation, with severe cases requiring a staged procedure. Early hypospadias repair with outpatient surgery helps to avoid separation anxiety and fears related to genital surgery.

VIII. ANESTHESIA

A. Hypospadias surgery is performed under general anesthesia.

B. A penile nerve block or a caudal supplementation is standard to minimize postoperative discomfort.

C. Prospective studies have not shown an increase risk of cognitive or developmental abnormalities in children undergoing general anesthesia early in childhood.

IX. HYPOSPADIAS OPERATIONS

The literature is filled with hundreds of different hypospadias surgeries. The list below is a contemporary summary of the present surgical approach.

A. Primary tubularization (GAP, Thiersch-Duplay, King, Pyramid) (Fig. 2-2).

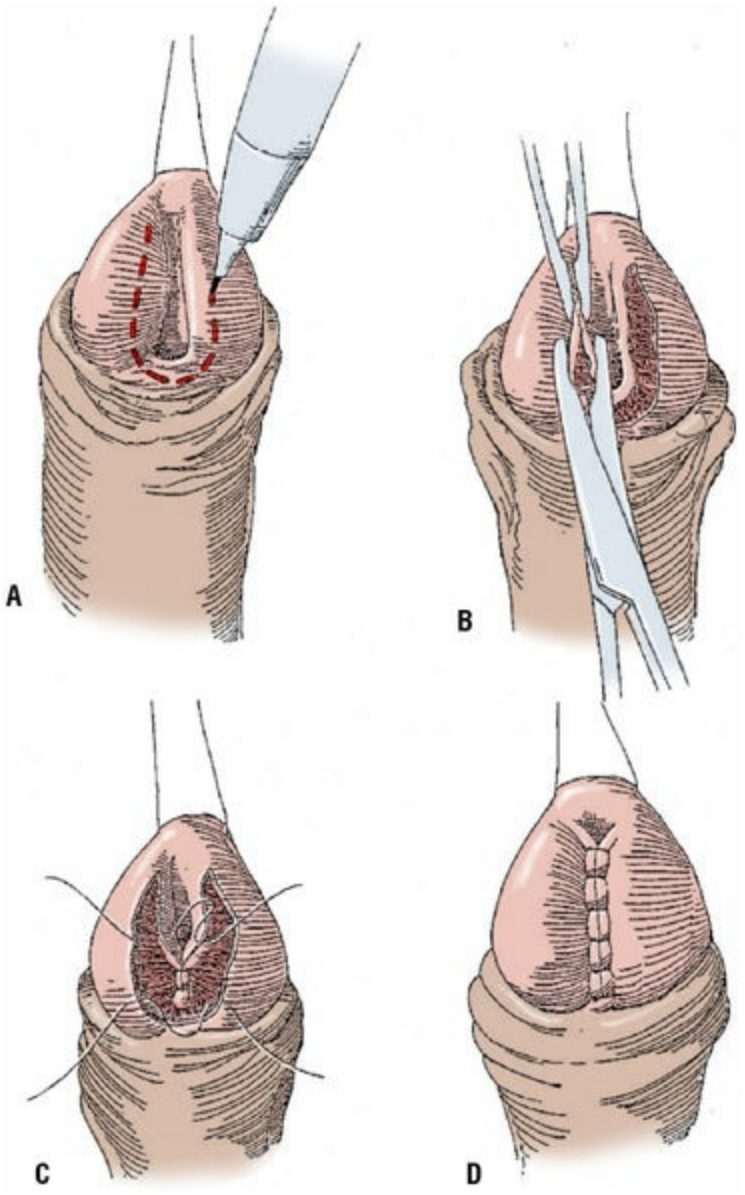

Fig. 2-2 A–D GAP hypospadias repair.

B. Meatal advancement and glanuloplasty procedure (MAGPI) (Fig. 2-3).

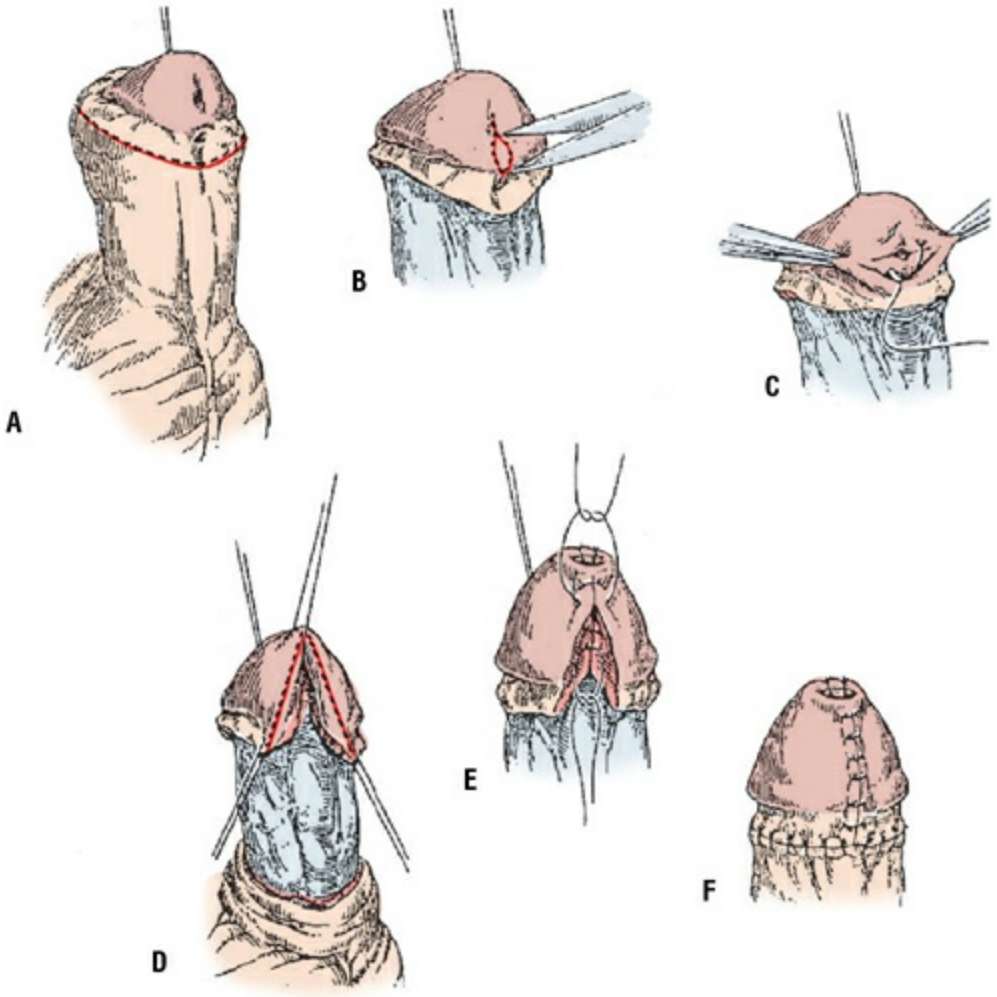

Fig. 2-3 A–F MAGPI hypospadias repair.

C. Primary tubularization with incision of the urethral plate (Snodgrass) (Fig. 2-4).

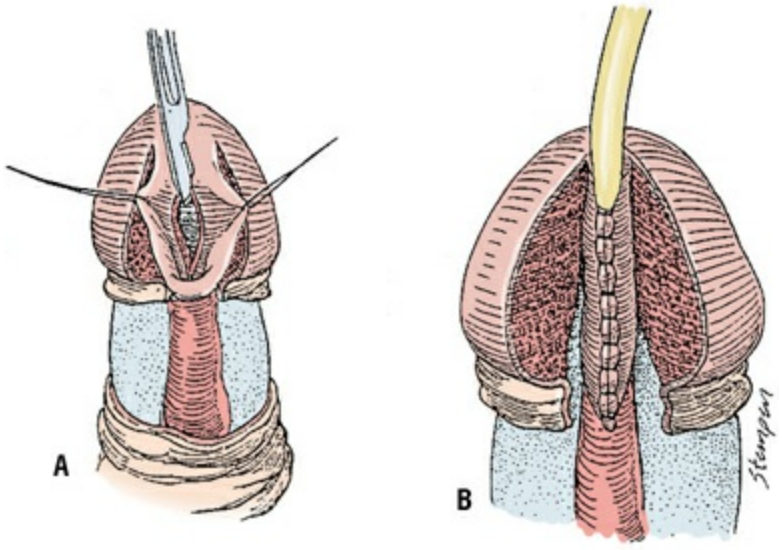

Fig. 2-4 A–B Hypospadias repair with incision of the urethral plate (TIP repair).

D. Onlay island flap procedure (Fig. 2-5).

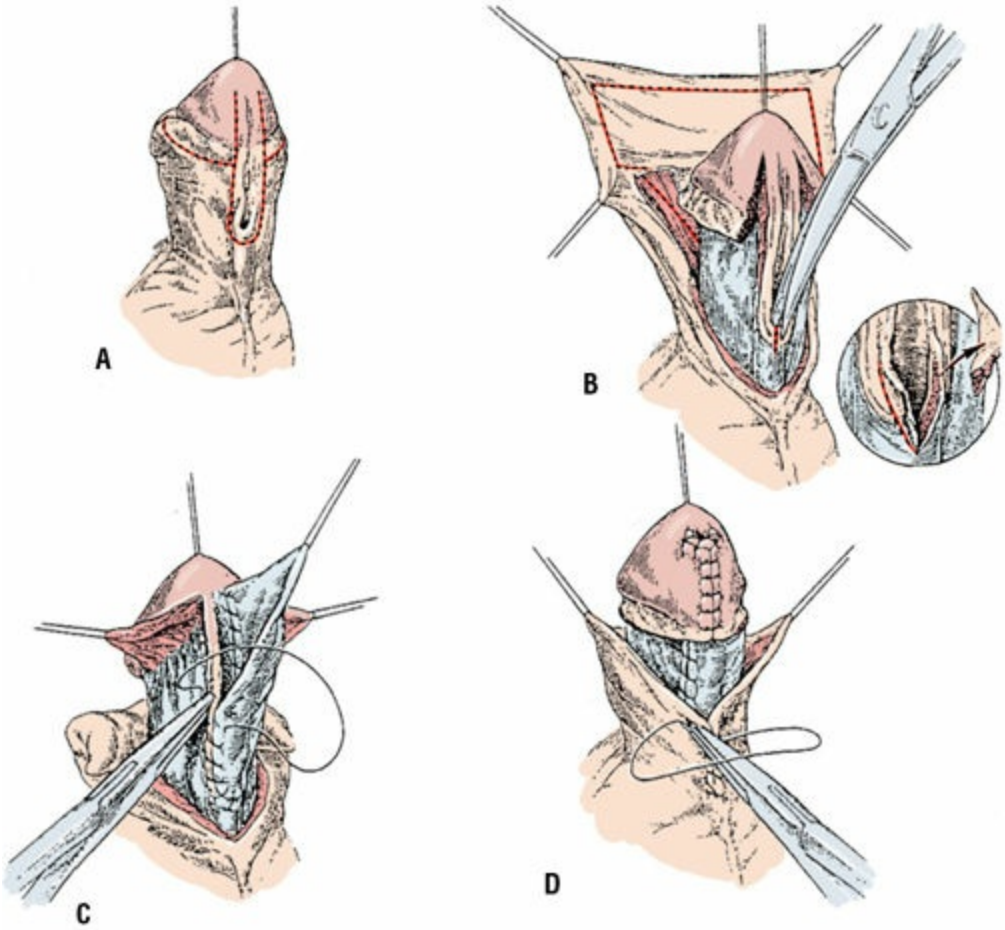

Fig. 2-5 A–D Onlay island flap hypospadias repair.

E. Staged repairs: In patients with severe hypospadias, two planned operations approximately 6 months apart yielding a controlled outcome with less complications has become fashionable. The first stage consists of penile straightening and the transfer of vascularized skin from the excess prepuce from the dorsal to the ventral aspect of the penis. The second stage consists of the reconstruction of the new urethra, glans penis, and skin.

F. Salvage repairs with buccal mucosa grafts (taken from the inside of the cheek) can be used for urethral replacement typically in a secondary procedure when local vascular flaps have failed and there is a paucity of excess penile skin (Fig. 2-6).

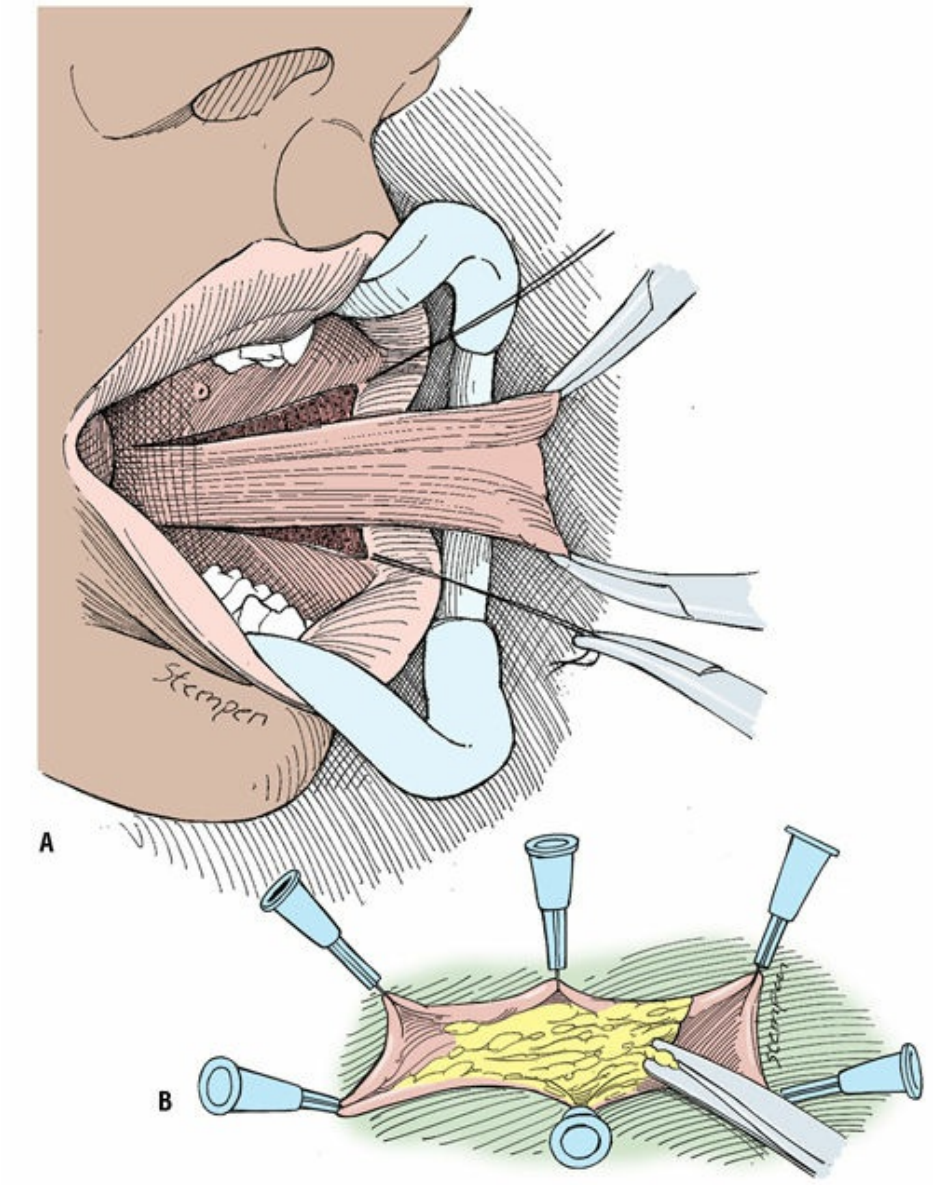
A
B
Urethral scar removed and buccal graft tissue replaced
Second stage urethroplasty and closure of buccal mucosa
Allow > 6mos of healing between surgeries
Completed repair
C
D
E

Fig. 2-6 A: Buccal mucosa free graft harvest. B: Preparation. C: Placing buccal mucosa graft after removing scar tissue. D: Second-stage surgery after 6 months creating a new buccal urethra. E: Completed repair.

G. Straightening the penis can be performed with a midline dorsal tunica plication procedure that does not violate the nerve supply, hence preserving normal erectile function (Fig. 2-7).

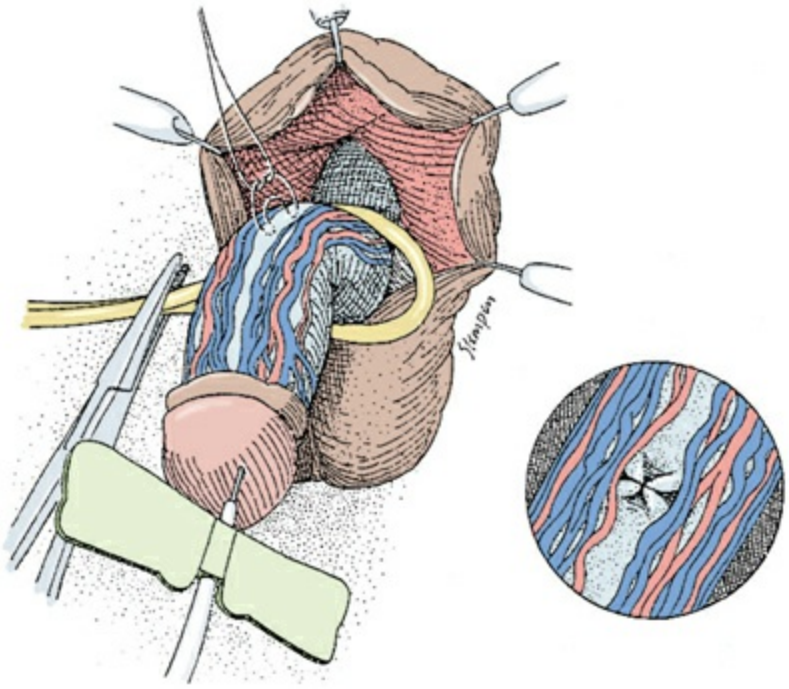

Fig. 2-7 Dorsal plication for the correction of penile curvature.

X. COMPLICATIONS OF HYPOSPADIAS SURGERY

A. Urethral Cutaneous Fistula

1. Urethral cutaneous fistula consists of a communication between the new urethra and the penile skin, allowing the urine to come out through two separate holes.
2. Fistulas require operative closure approximately 6 months after the initial operation when tissue swelling has subsided.

B. Meatal Stenosis

1. This is a stricturing of the new urethra which can

occur anywhere along the urethroplasty, but most commonly occurs in the glans penis.

C. **Urethral Diverticulum**
   1. This is a large outpouching or ballooning of the urethra secondary to too large of a urethroplasty or an obstruction distally (i.e., meatal stenosis).

D. **Superficial Skin Loss**
   1. This is a relatively common complication after hypospadias surgery and typically will heal spontaneously without the need for further surgical intervention by secondary penile skin granulation. This can be treated with local wound care and daily bathing.

E. **Residual Penile Curvature**
   If severe, reoperation with penile straightening is required.

XI. POSTOPERATIVE HYPOSPADIAS CARE

A. Anterior hypospadias repair such as the MAGPI and GAP are often done without the use of a drippy stent, or stent for 48 hours along with pain medication.

B. More severe hypospadias requires the use of an indwelling drippy stent which is typically removed 7 to 14 days after surgery by cutting a stitch that secures the urethral catheter to the glans penis (Fig. 2-8).

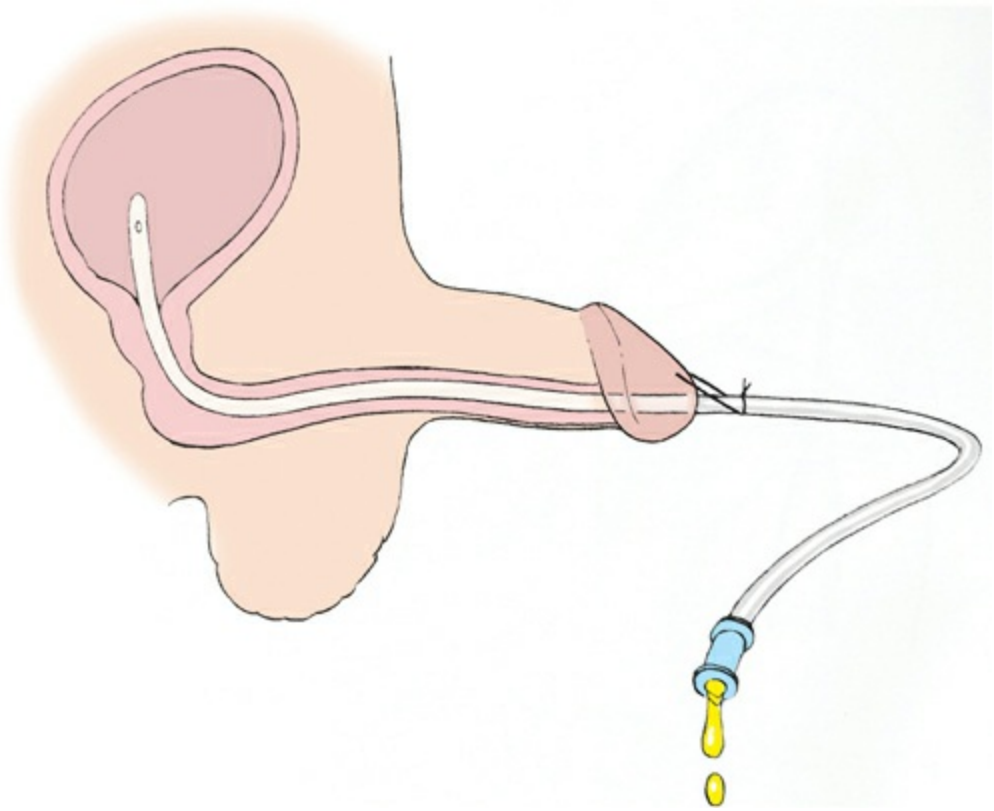

Fig. 2-8 Urinary diversion drippy stent for hypospadias repair.

C. Prophylactic doses of antibiotics (see Chapter 33) such as Bactrim or nitrofurantoin are typically prescribed while the stent is in place to keep the urine sterile.

D. Postoperative symptoms include the following.
   1. Bladder spasms, which can be treated with oxybutynin (Ditropan).
   2. Urinary retention, which is uncommon but can occur secondary to a stent malfunction such as blockage or kinking.
   3. Postoperative pain, which is controlled with acetaminophen (Tylenol), Hydrocodone, and antiinflammatory agents such as Motrin.

E. Dressings: The most common dressing used after hypospadias is a plastic dressing such as Tegaderm which is used with gauze to sandwich the penis onto the abdomen and is typically removed at home 2 to 3 days after surgery.

XII. POSTOPERATIVE HYPOSPADIAS CARE

A. The majority of cases of patients with hypospadias can expect good outcomes with one operation. The reconstruction tends to grow with the child and results in a normal phallus for voiding, appearance, and sexual function after puberty.
B. To ensure patient satisfaction and an understanding of their congenital anomaly, my practice is to see patients who have had hypospadias reconstruction 1 year after the repair, after toilet training, and after puberty.
C. Patients with the most severe forms of hypospadias can have long-term issues and need closer follow-up.
D. Patients with complications are seen as required. With better primary techniques the goal is to eliminate the need for salvage surgery.

RECOMMENDED READING

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3 Undescended Testes—Cryptorchidism

Guy A. Bogaert

I. Definition

The testis is “undescended” if it is not in the scrotum or cannot be brought there during physical examination.

Cryptorchidism means hidden or obscure testis in Greek and is often used interchangeably with the term “undescended testis.” However, a cryptorchid testis may be atrophic or ectopic as opposed to truly undescended.

From a clinical point of view, the testis may be palpable or nonpalpable.

A. A testis which is not in the scrotum on physical examination is either palpable elsewhere or nonpalpable. A palpable testis may be found along the normal descending pathway (truly undescended, exiting the abdomen at the internal inguinal ring in the direction of the external inguinal ring), or ectopic outside the normal pathway (perineal, femoral, prepenile) (Fig. 3-1).

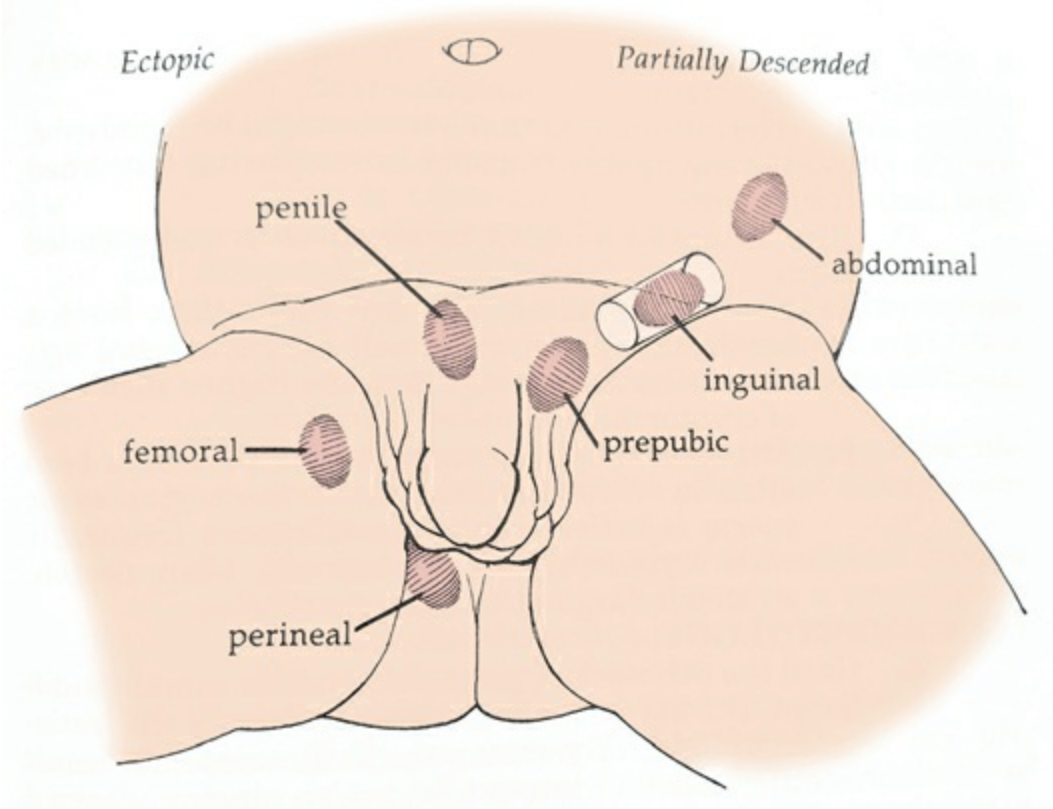

Fig. 3-1 Patient's left side depicts normal pathway for testicular descent illustrating possible locations of undescended testes. Patient's right side shows possible locations of normal testes that descend into an ectopic position.

B. A testis outside the scrotum, but palpable, can be *retractile* (not truly undescended), *incompletely descended* (within the inguinal canal or just outside), or *ectopic* (following a different pathway, e.g., perineal, femoral).
C. The inability to palpate a testis (nonpalpable) means the testis is beneath the external oblique fascia (unusual), in the abdomen, or atrophic/absent.

A boy with a unilateral normal descended testis has the same paternity chance as a boy with bilateral normal descended testes (90%). Paternity rate in bilateral undescended testes is 62%.

The incidence of bilateral undescended testes is 5% to 15% of all boys with undescended testes.

II. CLASSIFICATION

A. A retractile testis is not truly undescended and is mostly palpated in the inguinal area. A retractile testis has an extrascrotal position intermittently because of an active cremasteric reflex. By definition, retractile testes function normally and do not require any form of treatment. In rare cases, a retractile testis can become "ascended," and may eventually require treatment.

B. An ectopic testis (Fig. 3-1) (less than 5% incidence) descends properly until misdirected outside the external inguinal ring, presumably by an abnormal gubernaculum. These testes may be found in the perineum, prepenile, or femoral areas. These testes are thought to be more normal than incompletely descended testes.

C. An incompletely descended testis (Fig. 3-1) (95% incidence) can be intra-abdominal, in the inguinal canal, or just exiting the external ring (prescrotal).

D. An absent or atrophic testis is uncommon (3.3% of all cryptorchid testes, likely the result of perinatal torsion).

III. INCIDENCE

A unilateral cryptorchid testis is among the most common congenital anomalies in boys and the most common surgical condition in pediatric urology.

A. **The Undescended Palpable Testis**

1. Newborns have an incidence of 3% to 5% of cryptorchidism (of those, 15% are bilateral).
2. Serial studies at 3 and 9 months of age have shown that most of these cryptorchid testes descend spontaneously.
3. By the age of 1 year, only 0.7% to 1% of these children will still have a cryptorchid testis (palpable along the expected descending pathway).
4. The same incidence of 0.7% has been found in young adults (military recruits), suggesting that no spontaneous descent occurs after 9 months of age.

B. **The Nonpalpable Testis**

1. In 20% of all children with a cryptorchid testis, the testis will be nonpalpable; however, only 25% of those will ultimately prove to be absent at surgical exploration.
2. In most cases (75% of all patients originally with a nonpalpable testis), a nonpalpable testis will be intra-abdominal, or depending on the experience of the examiner, in the inguinal canal.

C. **Risk Factors for a Higher Incidence of an Undescended Testis**

1. Newborn children who are premature, have a low birth weight, are small for gestational age, or twins have a significantly higher incidence of cryptorchidism.
2. Although it has been suggested that boys born after in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) would present more frequently with cryptorchidism, this has not been demonstrated in large epidemiologic studies.

D. **The Ascending Testis**

Boys, commonly aged 5 to 12 years of age, with a history of normal or retractile testis can present at this age with an "ascended" testis. These boys previously had a normal descended testis that has now become undescended. The etiology of the ascending testis is unknown but may be secondary to a large growth spurt or a persistent patent processus vaginalis. Ascended testes usually require surgical correction.

IV. EMBRYOLOGY

A. Until the 6th week of gestation, the gonads remain indifferent. During weeks 6 and 7, the effects of the testis determining factor (TDF) protein from the SRY gene (on the Y chromosome), result in differentiation into a testis. Also, in weeks 6 and 7, Sertoli cells develop and secrete müllerian inhibitory substance (MIS) that cause müllerian

duct regression. From the 9th week of gestation, Leydig cells produce testosterone, which stimulates Wolffian duct development.

B. Testicular descent usually occurs in the third trimester (it has been documented by prenatal ultrasound that no descent is seen before 28 weeks gestation).

V. ETIOLOGY

Many theories have been proposed to explain the etiology of cryptorchid testes.

A. **Abnormality of the Gubernaculum Testis**
   1. The gubernaculum is a cordlike structure that extends from the lower pole of the epididymis and the testis to the scrotum.
   2. It appears that the gubernaculum does not pull the testis into the scrotum but rather guides it by providing a space into which the testis can descend.
   3. Absence or abnormality of the gubernaculum may be a cause of maldescent.
   4. An ectopic testis is likely to be secondary to an abnormally positioned distal extension of the gubernaculum, leading the testis to an abnormal position.

B. **Reduced Intra-abdominal Pressure**
   1. Overall, it is doubtful that diminished intra-abdominal pressure is an etiologic factor in most cases of cryptorchidism.
   2. All patients born with the prune belly syndrome have intra-abdominal testes.
   3. These may be due to reduced intra-abdominal pressure, but may also relate to a mass effect from bladder distension.
   4. In a similar experiment of nature, patients with gastroschisis have a higher incidence of cryptorchidism.
   5. However, these patients have central nervous system

abnormalities also, suggesting the possibility of pituitary or other endocrine dysfunction that may lead to incomplete descent.

C. **Abnormal Testis (Inborn Error)**
    1. This hypothesis originates from the observation that a lower fertility rate is common even after successful orchidopexy (fertility rate does not equal paternity rate).
    2. Therefore, congenitally abnormal testes from otherwise healthy newborns might not descend normally.
    3. However, it has been shown in animal studies that a normal testis is not even a prerequisite for testicular descent: a testicular prosthesis will descend in place of a testis.

D. **Endocrine Abnormality (at Testicular Level)**

Most likely an endocrine abnormality is the primary cause of cryptorchidism in the majority of healthy newborns. Human chorionic gonadotropin (hCG), testosterone (T), dihydrotestosterone, calcitonin gene–related peptide, epidermal growth factor, insulin-like 3 (INSL-3), inhibin, and luteinizing hormone (LH) all may influence directly or indirectly the process of testicular descent. Hence an abnormality in one of these may result in cryptorchidism. In fact, several studies have shown reduced T and LH during the first 6 months of life in children with unilateral undescended testes. However, it is unclear how a generalized endocrinologic problem causes cryptorchidism on only one side. It is therefore suggested that the situation of hypogonadotropic hypogonadism is at the local testicular level.

VI. significance

A. **Cancer**
    1. Patients with a history of cryptorchidism or a truly undescended testis have an 8 to 30 times increased risk of testis cancer. The incidence of testis cancer in

the general population is 6 per 100,000. Of all testis cancers, 11% will originate in cryptorchid testes.

2. If the surgical orchidopexy is performed after the age of 12 years, the risk of testicular cancer doubles compared to early orchidopexy.
3. The risk of developing testicular cancer is also increased in the normal contralateral testis, however not as high as in the ipsilateral testis.

B. **Fertility and Paternity**

1. The incidence of fertility problems after treatment is hard to judge scientifically, owing to the variability in the cause of the anomaly. By definition, fertility is determined by evaluation of sperm analysis from the ejaculate. In contrast, paternity is the ability to father a child and is more relevant and important. However, paternity is dependent on a combination of male and female fertility factors.
2. In general, the following information is known:
    a. The histologic appearance of the cryptorchid or undescended testis in children is less favorable than normal and deteriorates with age.
    b. Paternity rate in patients with a history of unilateral cryptorchidism or undescended testis is almost normal (89%) and therefore the results of semen analysis are of limited clinical importance.
    c. In patients with bilateral undescended testes, the paternity chance is reduced to 60% (compared to 85% to 90% in the normal population) and the semen analysis is abnormal in 50% to 75% of patients.
    d. Several studies have shown a germ cell loss at 12 to 14 months of age, suggesting surgical correction before this age in hopes of preserving normal germ cell function, even in unilateral cases.

C. **Associated Findings**

1. A cryptorchid testis is more mobile and therefore more prone to torsion. Due to its frequent location just in front of the symphysis, the undescended testis is theoretically more susceptible to trauma but this is not documented in the literature.
2. The psychological effects of the undescended testis are not well known, but are probably not as important as penile abnormalities.
3. Also, the majority (up to 80%) of children with a cryptorchid or undescended testis will have a patent processus vaginalis (indirect inguinal hernia).

VII. DIAGNOSIS

The diagnosis of cryptorchidism is made after physical examination and consideration of the patient's medical history. There is no role for radiographic imaging in the diagnosis of cryptorchidism.

If a child has no testis in the scrotum, the most important task of the examining physician is to determine whether the testis is palpable (retractile and not truly undescended, inguinal, or ectopic) or nonpalpable (abdominal, inguinal, or absent-atrophic).

The history at birth is an important factor: for example, if both testes were present in the scrotum they are likely retractile.

A. Physical Examination

1. Although dependent on the experience of the examiner, the clinical examination is the most reliable, accurate, least invasive, and least expensive test for a child with a cryptorchid testis.
2. The best time to make the initial diagnosis of cryptorchidism is before 6 months of age. This is because the cremasteric reflex is weak in the newborn period and the overlying body fat is minimal. Of note is that a patient seen for an

undescended testis, who had a normal testis for the first 6 months of life, is likely to have a retractile and not a truly undescended testis.

3. Visually, the shape of the scrotum on the side of the cryptorchid testis can be an indication of whether the testis was ever present. A normal hemiscrotum suggests that the testis will be found below the internal ring.
4. Visual inspection of the inguinal, suprapubic, scrotal, and perineal region will find an ectopic testis.
5. In supine position, palpation should start well above the scrotum, usually in the region of the superior, anterior iliac crest. Then, a firm downward pressure (toward the sacrum) is applied as the examiner's hand moves obliquely toward the symphysis. While the examiner maintains this downward pressure (toward the sacrum, not toward the feet), the opposite hand is used to palpate the ipsilateral scrotum. Lubrication with soap or gel on the fingers can improve the sensitivity of the clinical examination, especially in nonpalpable testes.
6. The optimal position to diagnose a retractile testis is the frog-like position (see Fig. 3-2). The child will prefer this position as opposed to the supine position as he can view what is happening. Talking to the child or the parents will reassure and distract the child. Then the tops of the fingers are brought behind the scrotum toward the front to inspect the content of the scrotum.

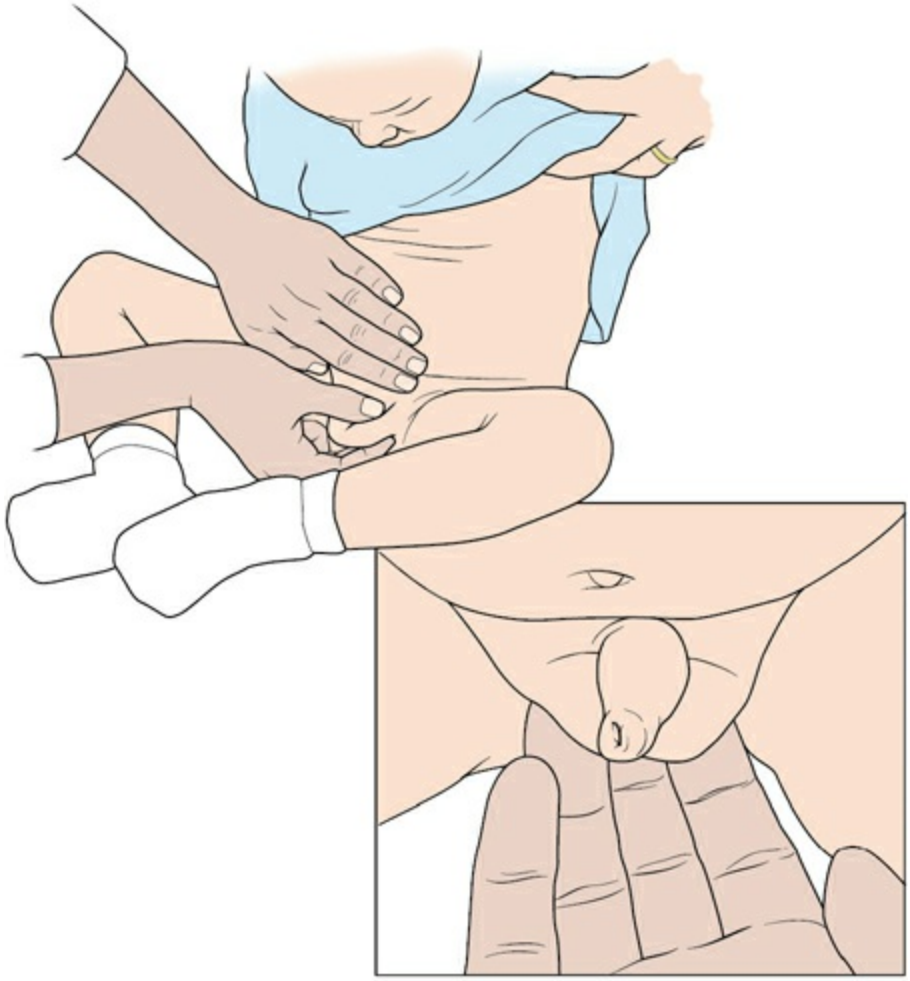

Fig. 3-2 A boy in frog-legged relaxed position with the fingers of the examiner behind the scrotum demonstrating bilateral retractile testes.

7. It is unreliable to have the family check for the testis in the bath or other circumstances.
8. Repetitive examination or referral to an experienced examiner can avoid additional and invasive diagnostic procedures and also reduce confusion or differentiation between an undescended (and in some cases, nonpalpable) testis with a retractile testis.

B. **Imaging Studies**

In essence, the clinical examination by an experienced examiner is the most important and reliable examination to differentiate between a palpable and nonpalpable testis. As noted above, there is generally no role for radiographic imaging in the diagnosis of cryptorchidism.

Ultrasound imaging studies are popular, but are not helpful. Although noninvasive, there are frequent false negative and false positive results, which preclude its clinical usefulness. Similar findings are seen with arteriography, computed tomography (CT), or magnetic resonance imaging (MRI) scanning. In addition, if a testis is found on imaging, surgery is recommended and if not, the sensitivity is not enough to prevent operative exploration.

Laparoscopy is the most reliable technique to localize a nonpalpable testis or prove its absence (vanishing testis). Although it requires general anesthesia, it is a safe and accurate procedure in the hands of an experienced examiner. In addition, the laparoscopic findings will define the next operative step. This means that laparoscopy is both a diagnostic and/or therapeutic tool.

C. **Hormonal Evaluation**

1. Undescended testes are considered a form of endocrinopathy, as there may be a defect in the hypothalamic-pituitary-testicular axis and a higher incidence in the presence of environmental endocrine disruptors. However, hormonal evaluation is of debatable usefulness.
2. In the situation of true bilateral nonpalpable testes, a pelvic ultrasound can detect possible müllerian structures (uterus) and a chromosome and hormonal analysis is essential. Girls with congenital adrenal hyperplasia may be fully virilized and present as boys with an empty scrotum. To prove anorchia, there must be a high baseline luteinizing hormone (LH) and follicle stimulating hormone (FSH) as well as a low testosterone and no testosterone response to a prolonged trial of human chorionic gonadotropin (hCG). If these criteria are completely met, anorchia is most likely and laparoscopic confirmation may be postponed until puberty, when testicular prostheses are likely to be placed. Otherwise, surgical

exploration at around 6 months of age is recommended.

VIII. THERAPY

The rationale for treatment of patients with cryptorchidism is based on limiting complications and correcting the associated findings. Preservation of germ cell deterioration and reducing the chance of developing malignancy are the main considerations, although the chance of torsion, trauma, and the psychological aspect of missing a testis also play a role. In addition, the high incidence (80%) of an associated patent processus vaginalis in patients with undescended testis also requires surgical correction.

Although intuitive, there are limited data demonstrating that early surgery reduces complications.

A. **Hormonal Therapy (before or after Surgery, or None)**

In a large meta-analysis of published data using hCG or luteinizing hormone-releasing hormone (LHRH) in an attempt to treat undescended testes, the successful descent rate was 12%, which was not considered significant. It may be useful in rare children with high operative risk.

Some investigators have proposed hormonal stimulation (LHRH in a low, once every second day dosage) after successful orchidopexy in an effort to treat the theoretical hypogonadism that may limit germ cell maturation and hence fertility. Although it has been shown to improve histology in the short term, there are very limited data suggesting improved fertility or paternity.

B. **Surgery**

1. Operative treatment should be undertaken early, between 9 and 18 months of age for palpable testis. This is after the time where most spontaneous descent would have occurred (between 0 and 9 months) and before germ cell deterioration may

occur. Also, from a psychological point of view, it is well accepted that children do better with genital surgery before the age of 18 months. There is less separation anxiety and less castration concerns.

2. Surgery for the palpable testis: It involves standard inguinal exploration and orchidopexy. Surgery for a palpable cryptorchid testis consists of a 3-cm inguinal incision (usually hidden in an inguinal skin crease), mobilization of the spermatic cord and testis, and ligation of the associated patent processus vaginalis. The testis is mobilized into a subdartos pouch in the scrotum. The procedure can nearly always be performed as an outpatient procedure with minimal morbidity (young children will be essentially normal within 2 days). The success rate is 99%. Also in the event of an ectopic testis, this inguinal approach is preferred as the spermatic cord must be mobilized and the testis can be brought into the scrotum via this inguinal incision.
3. Surgery for the nonpalpable testis: Prepare to perform an inguinal incision or a laparoscopy. The child is reexamined while under anesthesia; if the testis has become palpable, an inguinal incision is performed. If the testis remains nonpalpable, a diagnostic laparoscopy is performed (some may still start with an inguinal incision). Surgery of intra-abdominal testes is technically challenging.
    a. A standard inguinal orchidopexy will only succeed in situations where the intra-abdominal testis is close to the internal inguinal ring and the child is young.
    b. Alternatively, modifications have allowed good success in skilled hands by dividing the testicular vessels in one or two stages (known as the Fowler-Stephens procedure).
    c. Microvascular transfer was popular in the past but is not practiced currently.

d. In recent years, laparoscopy has become the treatment of choice in the approach of abdominal testes. In most centers, laparoscopy is performed to visualize the testis and plan the approach. The testis may be mobilized laparoscopically and brought into the scrotum with a minimum of morbidity and as an outpatient procedure. In some cases, the testis is too high and the spermatic vessels must be divided in order to provide sufficient length. In these cases, the collateral blood flow from the vas deferens must be carefully preserved and keeps the testis alive in most instances (one- or two-stage Fowler-Stephens procedure). This can be performed laparoscopically.

e. A removal of the intra-abdominal testis is recommended currently if an abdominal testis is found in a boy older than 10 years, with a normal contralateral descended testis (EAU-ESPU, German, and AUA guidelines). In these cases, the chance of the testis contributing to fertility is minimal and the testis is still prone to malignancy, therefore orchiectomy is advised.

IX. SUMMARY

- A well-documented physical examination at birth is an important factor in the diagnosis of a cryptorchid testis.
- The clinical examination in frog-legged relaxed position is the most reliable examination to differentiate a retractile testis from a truly undescended testis.
- The clinical examination is the most important factor to determine the eventual surgical indication (palpable/nonpalpable) and ultrasound is not helpful and should not be routinely performed.
- In the event of a nonpalpable testis, a laparoscopic exploration is the most reliable diagnostic tool.
- Awareness of ascending testis between the ages of 5 and 10

years is important.

- The benefit of hCG or LHRH to facilitate descent of a truly undescended testis is minimal to none.
- Surgical (inguinal) orchidopexy should be performed preferentially before the age of 12 months.
- For high intra-abdominal testis a Fowler-Stephens procedure (interrupting and transecting the testicular vessels) in one or two stages is the treatment of choice.
- Men with a history of unilateral undescended testes have normal paternity whereas those with a history of bilateral undescended testes have reduced paternity.

RECOMMENDED READING

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4 Abnormalities of Sex Differentiation

Jason M. Wilson

Typical sex differentiation is an intricately choreographed processes involving chromosomally directed gene expression, protein and hormone production, gonadal development, and development of reproductive anatomy. An abnormality of sex differentiation is manifested when there is a misstep in the process, which may occur at any point in development, resulting in atypia of chromosomes, genes, gonads, hormones, and/or anatomy. As critical members of a multidisciplinary team, we may be called upon to evaluate the newborn with genital atypia or, more rarely, when phenotype is not consistent with antenatal karyotype. Abnormalities of sex differentiation may also be diagnosed with newborn screening or during a workup for illness or for either early or delayed secondary sex characteristics.

I. TYPICAL SEX DIFFERENTIATION

Sex determination has long been attributed to X and Y "sex chromosomes," but observations in patients with Turner syndrome led to the hypothesis that the genetic material responsible for testis development was located on the Y chromosome. Further investigations suggested that the specific region was located on the short arm of the Y chromosome, and in the 1990s, the sex-determining region (SRY) of the Y chromosome was mapped. Female sex determination is dependent on two functional X chromosomes and is a much

more complex process than previously believed. Sex differentiation is the process wherein bipotential embryonic tissue becomes sex-dichotomous: gonadal tissue, internal genitalia, and external genitalia. The presence of either 46,XX or 46,XY karyotype determines sex-specific development in bipotential cells.

II. EMBRYONIC DEVELOPMENT

By the third week of embryonic development, gonadal development proceeds from the indeterminate mesoderm (gonadal ridge) and then continues medial to the mesonephros (mesonephric ridge). The gonadal ridge is further differentiated into a nourishing and sustaining environment for gonadal development by the arrival of primordial germ cells (PGCs) by the fifth week of embryonic development. Under the direction of gene expression and transcription factors, the arriving PGCs differentiate into four types of bipotential cells that compose the bipotential gonad: germ cells, steroidogenic cells, supportive cells, and connective tissue. By the fifth to sixth week of bipotential development, the gonadal ridge, mesonephric duct (wolffian), and paramesonephric duct (müllerian) have developed. The coelomic epithelium has invaginated craniocaudally to form the müllerian duct. The invagination actually extends down to the uterovaginal sinus, where the two ducts meet and fuse to form the uterovaginal duct in both sexes. Figure 4-1 represents sex-specific differentiation from bipotential gonadal and ductal tissue.

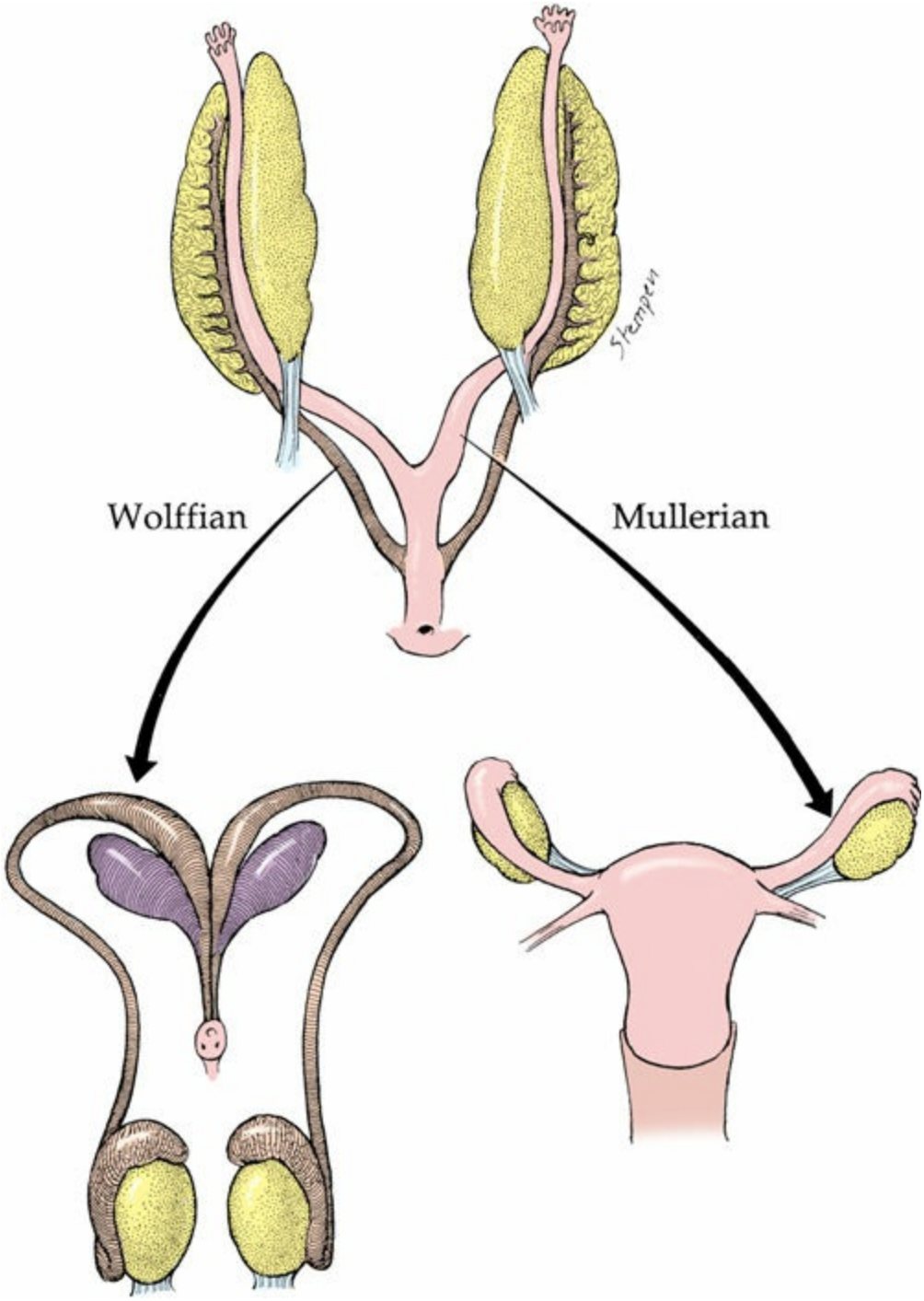

Fig. 4-1 Embryologic development of both the male and female reproductive tracts from a common origin.

III. 46,XY GONADAL AND DUCTAL DEVELOPMENT

The earliest discernible change in the development of the testes is formation of the testicular cords at six to seven weeks

of development. This early differentiation is responsible for the development of the seminiferous tubules and Sertoli cells. Other cells among the testicular cords differentiate into Leydig cells between eight and nine weeks of development. Still other PGCs differentiate into male sex-specific germ cells (spermatogonia). By eleven weeks of development, recognizable testes are present with Sertoli, Leydig, and male sex-specific germ cells.

A. **Endocrine Function**
    1. Endocrine function of the fetal testes is responsible for sex-specific ductal development and regression. Between seven and eight weeks of development, the Sertoli cells secrete müllerian-inhibiting substance (MIS), a paracrine hormone that acts to stimulate regression of the ipsilateral müllerian (paramesonephric) ducts. In typical male sex-specific differentiation, the remnants of the müllerian ducts can be seen as the appendix testis and the prostatic utricle.

B. **Testosterone Production**
    1. Testosterone production from Leydig cells is detectable as early as nine weeks of development and peaks in the local environment by 13 weeks. During this period, it is produced autonomously, independent of placental human chorionic gonadotropin (hCG) and luteinizing hormone (LH) and is responsible for further development of the wolffian (mesonephric) ductal system into the internal male reproductive tract: epididymis, vas deferens, seminal vesicle, and ejaculatory duct. The conversion of testosterone to dihydrotestosterone by 5α-reductase is necessary for further male sex-specific anatomy, including the prostate, urethra, and external genitalia. The rate-limiting enzyme for production of testosterone within the fetal testes is 3β-hydroxysteroid dehydrogenase (3B-HSD).

IV. 46,XX GONADAL AND DUCTAL DEVELOPMENT

A. Ovarian Development

1. Ovarian development is thought to begin later than testis development at approximately eight weeks of embryonic development. Primordial germ cells arrive at the gonadal ridge by the fifth week of development with primitive sex chords that develop into the testicular cords in the presence of SRY expression. Likewise in the presence of SRY, the medullary cords differentiate into Sertoli cells and invest PGCs. In the absence of SRY, cortical cords develop and invest PGCs. In the absence of SRY, there is development of the cortical cells that invest PGCs (follicle cells), forming ovarian follicles. Differentiation of the bipotential cells in the gonadal ridge into the fetal ovary is complete by as early as fourteen weeks of development. Estrogen is detectable by eight to nine weeks of development. The rate-limiting enzyme for estrogen production in the fetal ovary is aromatase. The absence of MIS and testosterone in the presence of active female gene expression leads to the dissolution of the mesonephric (wolffian) ducts and elongation of the paramesonephric (müllerian) ducts by about the ninth week of development. The müllerian ducts give rise to the fallopian tubes, the uterus, and the upper two-thirds of the vagina. Embryologic remnants of the wolffian ducts can be found in the mesentery of the ovary as the epoophoron and the paroophoron and at the anterolateral vaginal wall as Gartner duct cysts (Table 4-1).

V. DISORDERS OF SEX DEVELOPMENT (DSDs)

A. Proposed Nomenclature

Nomenclature from the 2006 consensus statement provides a flexible framework within which different

abnormalities of sex differentiation can be categorized. Instead of the term “disorder,” which is not preferred by some groups, more general or specific terms can be considered. For example, “abnormality or variation of reproductive development” may be used instead of “disorders of sex development” or “congenital adrenal hyperplasia” (CAH) in place of “46,XX DSDs.”

TABLE 4-1 Timeline for Typical Male and Female Sex Differentiation

Male	
3rd week	Primordial germ cells (PGCs)
4th week	Formation of the mesonephric duct Migrating PGCs Connection of the mesonephric duct with the cloaca
5th week	Subdivision of the cloaca into the rectum/urogenital sinus Gonadal ridge—arrival of PGCs Invagination and elongation of the müllerian duct
6th week	Invagination and elongation of the müllerian duct
7th week	Formation of the genital swelling Sertoli cells differentiate Formation of the urethral groove Formation of the gubernaculum Differentiation of the Leydig cells Formation of the genital tubercle Rupture of the cloacal membrane
8th week	Müllerian ducts regress (müllerian inhibitory substance)
10th week	Male phenotype is recognizable (testosterone) Fusion of the urethral folds Median raphe of the scrotum
12th week	Differentiation of the seminal vesicle and prostate

	gland
Female	
3rd week	Primordial germ cells (PGCs)
4th week	Formation of the mesonephric duct
	Migration of PGCs
	Connection of the mesonephric duct with the cloaca
5th week	Subdivision of the cloaca into the rectum/urogenital sinus
	PGCs colonize the genital ridge
	Formation of the müllerian duct
7th week	Formation of the urethral groove
	Formation of the anal and urogenital folds
8th week	End of the indifferent gonads in the female
	Dissolution of the mesonephric ducts
9th week	Female phenotype is recognizable
	The müllerian ducts join at the distal end and form uterovaginal duct
12th week	Differentiation of the accessory sex glands (Bartholin and Skene)

B. **Evaluation**

Evaluation of the child with a suspected abnormality of sex differentiation should be undertaken by a multidisciplinary team consisting of endocrinologists, genetics/dysmorphology specialists, urologists psychiatric specialists, and social workers. It is useful to have a point person to communicate regularly with the family and possibly to have care conferences with family and providers throughout the process of evaluation, diagnosis, and recommendations. Figure 4-2 illustrates the ways in which a suspected DSD is encountered.

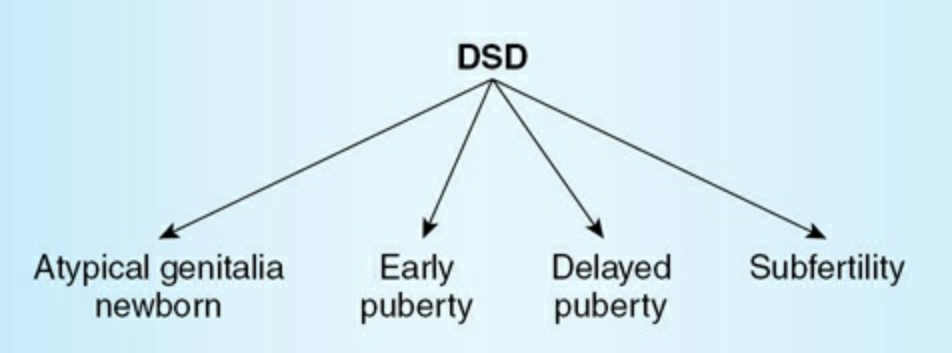

Fig. 4-2 Different presentations of DSDs.

VI. HISTORY

A thorough history should be obtained, including maternal medical history, family history, and whether any similar conditions have been seen in other family members. In addition, any medications taken during the gestational period or any signs of maternal virilization should be specified. Specific aspects of family history that should be recorded include infant death, amenorrhea, hirsutism, infertility, and known occurrences of specific disorders.

A. Physical Examination

A physical examination should include inspection for general appearance and any signs of external abnormalities of development such as hemihyperplasia or other morphologic features known to be associated with specific diagnoses. The abdominal and perineal examination should include palpation for abdominal or pelvic masses and careful assessment of external genitalia, including phallic size (stretch length), and whether or not there are one or two palpable gonads in the inguinal area, scrotum, labia, or perineum. An abnormal penile stretch length for a full-term male infant is less than 2.5 cm (Table 4-2). It is important to remember that gestational age at birth affects phallic size. The palpation of a gonad during the physical examination effectively rules out any disorder of androgen excess under the broad category of 46,XX DSDs.

TABLE 4-2 Stretched Penile Length

Age	Range (cm)
Newborn (30 wk)	1.7–3.2
Newborn (34 wk)	2.2–3.8
Newborn (term)	2.7–4.3
<1 y	2.3–5.9
1–3 y	3.1–6.9
3–1 y	3.7–8.6
Adults	10.1–16.5

B. **Laboratory Evaluation**

Metabolic derangements that may be present in CAH may cause hyponatremia, hyperkalemia, and metabolic acidosis, all of which can be assessed with a basic metabolic profile. Signs and symptoms of CAH in the newborn may not be present until the second week of life. Serum measurement of 17-hydroxyprogesterone (17-OHP) after the first 48 hours of life can confirm the diagnosis of 21α-hydroxylase deficiency. Specific serum immunoassays can be ordered if another enzymatic defect is suspected in the patient with adrenal hyperplasia. Serum immunoassays are widely available and easy to attain. The workup of any patient suspected to have an abnormality of sex differentiation should include serum levels of testosterone, estradiol, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and MIS. An hCG stimulation test may be useful if used for a specific purpose. Undetectable levels of MIS suggest the absence of testicular tissue.

C. **Genetic Testing**

A karyotype from a peripheral blood sample should be obtained in any patient with a suspected abnormality of sex differentiation. Fluorescent in situ hybridization to assess for the presence of the Y chromosome or SRY can be completed within 48 hours. If chromosomal occult

mosaicism is suspected, it may be necessary to send biopsies from gonadal tissue for cytogenetic evaluation. Advances in clinical genetic testing have made tests such as chromosomal microarray (CMA) widely available. CMA determines sex chromosome complement, evaluates for the presence of SRY, and screens for known duplication or deletion anomalies associated with DSDs; it is especially useful when a syndromic diagnosis is suspected.

D. **Imaging and Other Objective Data**

Sonographic examination of the abdomen and pelvis may be most useful in evaluating nondilated internal genitoreproductive structures. Ultrasound may demonstrate müllerian structures (vagina, uterus) in the newborn if present but is not reliable for demonstration of intra-abdominal gonadal structures. An abdominal ultrasound is also useful in screening for possible associated renal or collecting system abnormalities and enlarged adrenal glands encountered with CAH or other disorders of androgen biosynthesis. A genitogram is a voiding cystourethrogram of a common perineal opening, the urogenital sinus. It can be useful in assessing the length of the common channel associated with disorders in which a urogenital sinus is present on physical examination and may demonstrate the presence of müllerian structures.

E. **Surgery**

Surgery is rarely useful in the newborn with suspected DSDs. Endoscopy of the urogenital sinus is commonly utilized as part of or when planning for vaginoplasty. It may also prove useful in inguinal hernia repair in a female patient or to assess for the presence of a proximal two-thirds vagina and cervix. If only the distal one-third of the vagina is present, diagnostic laparoscopy may be used to locate intra-abdominal testes. It may also be important in the situation of atypical gonadal development (mixed gonadal dysgenesis, ovotesticular DSDs).

F. **Sex of Rearing**

Sex of rearing should be recommended only after diagnosis, evaluation, and treatment by a multidisciplinary team and after a complete discussion with the family. Cases in which sex of rearing is unclear are rare but have potentially complex implications in the process of sexual development such as gender assignment, gender awareness, gender identity, and gender orientation. In these cases it may be prudent to recommend a nonspecific sex of rearing (a gender-neutral name) and consider the implications of this decision (parental, family, social) until the child is 3 years of age, when he or she may be exhibiting some signs of gender behavior. Gender dysphoria is uncommon in some cases (46,XX DSD/21α-hydroxylase deficiency) but may be more common in cases in which there is some degree of dysfunction of the androgen receptor (partial androgen insensitivity). Principles to consider include genitoreproductive potential, sex-appropriate appearance, fewest medical/surgical interventions, gender identity, and sexual development. In the event of surgery, discussions should be held with the family and the surgical team. Each case and individual patient should be considered separately. There are accepted tenets to consider: early separation of components of urogenital sinus, preservation of neuroanatomically sensitive tissue, functional outcomes, and removal of atypical gonadal tissue in the presence of Y (SRY). There are authors that posit gender identity and sexual development are personal and nuanced decisions, involving multiple and unpredictable factors, and therefore, a sex assignment can be recommended but surgery should not be undertaken until patient input or decision making is available. Finally, until a compete genetic characterization of all androgen receptor defects is possible, it is useful to assess degree of androgen receptor function with androgen supplementation or hCG stimulation.

VII. DIAGNOSIS AND TREATMENT OF COMMON DISORDERS IN NEWBORNS

Some common diagnoses are discussed. The tables (see Tables 4-3 to 4-5) provide a more comprehensive overview of the possible diagnoses within each category with associated karyotype, genitoreproductive anatomy/pathology, and cancer risk and treatment.

A. 46,XX DSD Androgen Excess: 21α-Hydroxylase Deficiency

The most commonly encountered DSD is congenital adrenal hyperplasia. The newborn female with virilized external genitalia is the most common atypical genital appearance and may resemble a male with hypospadias and bilateral, nonpalpable testes; there may also be clitoral enlargement and labioscrotal fusion. 21α-hydroxylase accounts for 90% to 95% of CAH, in which the decreased enzyme activity leads to accumulation of 17- hydroxyprogesterone and decreased production of aldosterone and cortisol, resulting in hyperkalemia, hyponatremia, dehydration, and hypotension if diagnosis is delayed.

1. Diagnosis: Diagnosis is made by elevated plasma levels of 17-hydroxyprogesterone. Figure 4-3 provides a visual representation of androgen synthesis (P450c21=21α-hydroxylase). Mutations in the 21α-hydroxylase gene located on the short arm of chromosome 6 are responsible for the deficiency. There are two types of clinical pictures with 21α-hydroxylase deficiency: 75% salt-losing and 25% virilization only attributable to varying degrees of enzyme deficiency. Newborn screening tests have increased diagnosis in males and for nonclassic forms of congenital adrenal hyperplasia. Undiagnosed late-presenting males may have short stature and subfertility. Females with the nonclassic form of congenital adrenal hyperplasia may present later in

life with oligomenorrhea and hirsutism or occasionally are diagnosed after delivering an affected infant (Table 4-3).

TABLE 4-3 46,XX DSD

Disorder	Pathology	Incidence	Gonads	Interna
21α-Hydroxylase deficiency	Excess androgen	1 in 5,000 to 15,000	Ovary	Mülleri
11β-Hydroxylase deficiency	Excess androgen	1 in 100,000	Ovary	Mülleri
3β-Hydroxy steroid dehydrogenase deficiency	Excess androgen, mild	Rare	Ovary	Mülleri
Excess maternal androgens	Excess androgen	Unknown	Ovary	Mülleri
46, XX testicular DSD	SRY present 80%, Y sequence detectable 90%, 10% Y sequence not detectable,	1 in 20,000	Small, firm testis	Wolffia

SOX9	
	duplicate
RSPO1	
	absent?

DOC, 11-deoxycorticosterone; DHEA, dehydroepiandrosterone; SRY, sex-determining region Y; FSH, follicle-stimulating hormone; LH, luteinizing hormone; T, testosterone.

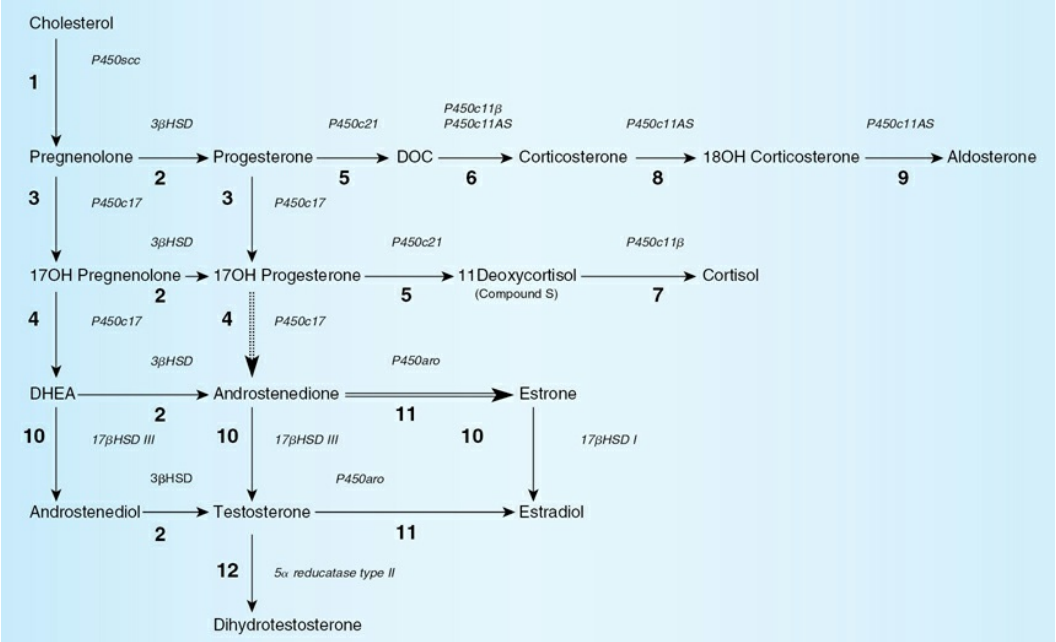

Fig. 4-3 Androgen synthesis.

2. Treatment: Treatment hinges on adequate glucocorticoid and mineralocorticoid replacement; adrenal crisis represents a medical emergency. Without adequate therapy, salt-losing will continue and virilization will progress. Therapeutic doses of glucocorticoid and mineralocorticoid replacement can be adjusted following serial measurements of electrolytes, androstenedione, and 17-hydroxyprogesterone. Evidence supports female sex rearing in even the most virilized patients, and proximal müllerian structures will have developed without atypia. Early vaginoplasty with separation of urogenital sinus components is undertaken with partial urogenital sinus mobilization for common

channel length less than 1.5 cm to 2 cm. Total urogenital sinus mobilization is usually necessary for common channel length greater than 2 cm. Procedural choice and technique for vaginoplasty are strongly influenced by surgeon experience. If clitoral reductive surgery is considered, it is critical to preserve the neurovascular bundle, glans tissue, and functional erectile tissue.

B. **Sex Chromosome DSDs: Mixed Gonadal Dysgenesis (MGD)**

After CAH, MGD is the most common etiology of atypical genital appearance in the newborn. The most common karyotype is 45,X/46,XY mosaicism. Less than 5% of DSDs can be attributed to ovotesticular DSD. The phenotypic spectrum ranges from that seen in 45,XO females to the typical male phenotype. When considering sex of rearing recommendation, the team must evaluate the degree of virilization present, the histology of the testes, and possibly the degree of phallic growth with testosterone or hCG stimulation. The streak gonad should be removed because of increased risk of malignancy. If the infant is to be male, the testes should be surgically fixed into the ipsilateral hemiscrotum. There may be increased risk of subfertility and malignancy.

C. **Sex Chromosome DSDs:Ovotesticular DSD**

Previously referred to as true hermaphroditism, ovotesticular DSD implies the histopathologic confirmation of both ovarian and testicular tissue. Most commonly this is an ovotestis (one gonad with both types of gonadal tissue), but it may rarely manifest as an ovary on one side and a testis on the other. Less than 5% of DSDs can be attributed to ovotesticular DSD. The most common karyotype is 46,XX, but up to one-third may be mosaic. The most common phenotype is male with posterior hypospadias, often resembling a urogenital sinus. Sex of rearing recommendation should be based on potential for genitoreproductive function, considering

internal and external anatomy. If an ovotestis or ovotestes is present, it may be possible to excise the discordant gonadal tissue, particularly if the gonad is compartmentalized or bipolar. Table 4-4 expands upon possible sex chromosome DSD. Sex of rearing recommendation should be based on the potential for genitoreproductive function, considering both internal and external anatomy.

TABLE 4-4 Sex Chromosome DSD

Disorder	Pathology	Incidence	Gonads	I
Klinefelter syndrome	Extra X and/or Y chromosome (47,XXY)	1 in 500	Small, firm testes Dysgenic seminiferous tubules	V
Turner syndrome	Only one functional X chromosome (45,X)	1 in 2000	Streak	N
Mixed gonadal dysgenesis	Incomplete müllerian regression Incomplete virilization (46,XY/45,X)	Second most common cause of newborn external genital atypia	Most commonly unilateral streak and contralateral testis undescended	V
Ovotesticular DSD	Ovarian and testis tissue present (46,XX; 46,XY;	Unknown	Unilateral ovotestis with ovary or testis	V

	46,XX/46,XY)	contralaterally (most commonly)

FSH, follicle-stimulating hormone; LH, luteinizing hormone; T, testosterone.

D. **46,XY DSD**

The list of possible diagnoses is extensive when considering the 46,XY newborn with atypical (undervirilized) external genitalia (Table 4-5). Diagnosis, evaluation, and treatment should proceed with input from the multidisciplinary team. Irreversible surgical procedures such as orchiectomy or gonadectomy should be avoided until an accurate diagnosis can be made. Most of the DSD in this category represents 46,XY karyotype and external genitalia along a spectrum of appearances ranging from typical female external genitalia to the male with hypospadias. It may be a manifestation of gonadal (testis) abnormality, a disorder of testosterone/hormone biosynthesis, receptor dysfunction, or enzyme deficiency (Table 4-6). Table 4-7 provides a summary of findings in common DSD diagnoses.

TABLE 4-5 46,XY DSD

Disorder	Pathology	Incidence	Gonad
Complete androgen insensitivity	Androgen receptor (AR) defect	1 in 20,000 to 1 in 64,000	Testis, usu intr abd
Partial androgen insensitivity	AR defect	Unknown	Testis
Leydig cell hypoplasia	LH receptor defect	Unknown, rare	Testis

46,XY pure gonadal dysgenesis (Swyer syndrome)	Unknown mutation prevents gonadal development	1 in 80,000	Streak
Absent testis (regression)	Mutation, teratogen	Unknown	Absen
Persistent müllerian duct syndrome	Defect in MIS production or receptor	Unknown	Testis
5α-Reductase deficiency	Defect in 5α-reductase2 action= low dihydrotestosterone	Rare with geographically specific increased prevalence	Testis
Steroidogenic acute regulatory protein deficiency	Cholesterol transport unable to occur Cholesterol does not get converted to pregnenolone Defect in testosterone synthesis	Rare	Testis
3β-Hydroxysteroid dehydrogenase deficiency	Defect in testosterone synthesis	Less than 1 in 100,000	Testis
17α-Hydroxylase deficiency	Defect in testosterone synthesis	Rare	Testis

17-20 Desmolase deficiency	Defect in testosterone synthesis	Rare	Testis
17β-Hydroxysteroid dehydrogenase deficiency	Defect in testosterone synthesis	Rare	Testis

AR, androgen receptor; hCG, human chorionic gonadotropin; MIS, müllerian inhibitory substance; FSH, follicle-stimulating hormone; LH, luteinizing hormone; DHEA, dehydroepiandrosterone; DOC, 11-deoxycorticosterone.

TABLE 4-6 Overview of 46,XY DSD Diagnoses and Associated Genital Appearance

Normal female external genitalia
Leydig cell hypoplasia
StAR (P450 cscc)
17α-Hydroxylase deficiency
17β-Hydroxysteroid dehydrogenase oxidoreductase deficiency
Complete androgen insensitivity syndrome
5α-Reductase deficiency
46,XY pure gonadal dysgenesis (Swyer syndrome)
Testicular regression
Varying degrees of incomplete virilization
StAR (P450 cscc)
P450 Oxidoreductase deficiency
3β-Hydroxysteroid dehydrogenase deficiency
17α-Hydroxylase deficiency
17,20-Lyase deficiency
Partial androgen insensitivity syndrome
Testicular regression/vanishing testes
Normal male external genitalia

Congenital adrenal hyperplasia
Partial androgen insensitivity syndrome
Persistent müllerian duct syndrome
Vanishing testes (testes disappear after first trimester)

TABLE 4-7 Summary of Findings in Common DSD Diagnoses

Genital Appearance	Karyotype	Gonads	Disorder
Atypical	46,XX	Ovary	21α-Hydroxylase deficiency
Atypical	46,XX	Ovary	11β-Hydroxylase deficiency
Atypical	46,XX	Ovary	3β-Hydroxysteroid dehydrogenase deficiency
Atypical	46,XX	Ovary	Excess maternal androgens
Atypical	46,XY	Testis	17β-Hydroxysteroid dehydrogenase deficiency
Atypical	46,XY	Testis	3β-Hydroxysteroid dehydrogenase deficiency
Atypical	46,XY	Testis	17-20 Desmolase deficiency
Atypical	46,XY	Testis	17α-Hydroxylase deficiency
Atypical	46,XY	Testis	Partial androgen insensitivity
Atypical	46,XY/46,X	Testis and streak	Mixed gonadal dysgenesis
Atypical	46,XX; 46,XY; 46,XX/46,XY	Testis and ovotestis	Ovotesticular DSD

Atypical	46,XX	Testis	46,XX testicular DSD, SRY negative
Atypical or female	46,XY	Testis	Leydig cell hypoplasia
Female	46,XY	Testis	Complete androgen insensitivity
Female	46,XY	Streak	46,XY pure gonadal dysgenesis (Swyer syndrome)
Female	46,XY	Absent	Absent testis (regression)
Female	46,XY	Testis	5α-Reductase deficiency
Female	46,XY	Testis	Steroidogenic acute regulatory protein deficiency
Male	46,XX	Testis	46,XX testicular DSD, SRY positive
Male	46,XY	Testis	Persistent müllerian duct syndrome
Male	47,XXY	Testis	Klinefelter syndrome
Female	45,X	Streak	Turner syndrome

5 Hydrocele, Hernia, Neonatal Torsion, and Scrotal Masses

Barry A. Kogan

Hydrocele and Hernia

I. DEFINITION

A. **Hydrocele:** An accumulation of fluid around the testicle. Types: Communicating and noncommunicating (Fig. 5-1 A–B).

1. Communicating: Persistence of a patent processus vaginalis with the same pathophysiology as an indirect hernia (see below) but a smaller opening, preventing bowel from entering. The fluid around the testis is peritoneal fluid. This is a congenital defect.
2. Noncommunicating: No connection to the peritoneum; rarer in children, occurs mostly in adolescents and adults. The fluid comes from the mesothelial lining of the tunica vaginalis and can be the result of inflammation of the testis or epididymis. This is an acquired lesion.

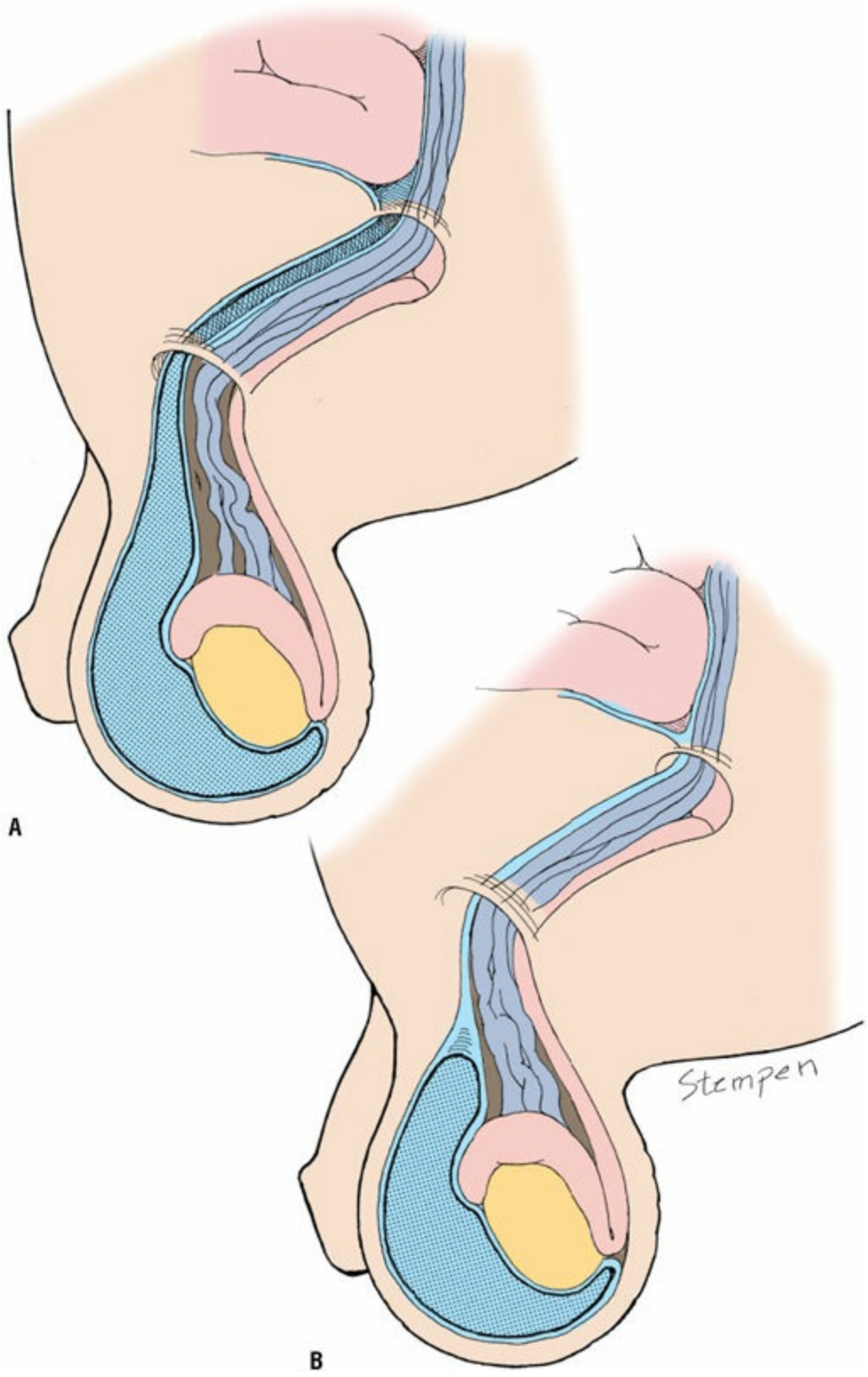

Fig. 5-1 Hydroceles. A: Communicating. B: Noncommunicating.

B. **Hernia:** A protrusion of an organ or tissue through an abnormal opening (Fig. 5-2).

Types: Indirect inguinal, direct inguinal, and femoral.

1. Inguinal, indirect: Persistence of a patent processus vaginalis. This defect is congenital and allows protrusion of peritoneal contents (usually omentum or small intestine) through the internal inguinal ring along the spermatic cord for a variable distance, and in some cases, as far as the scrotum. This may become incarcerated if it cannot be reduced back into the peritoneum. If so, the pressure of the hernia may alter blood flow to the testis, which can be damaged from ischemia. In addition, the blood flow to the bowel may be affected and, in this circumstance, it is called a *strangulated hernia*.
2. Inguinal, direct: Weakness in the floor of the inguinal canal. This is an acquired condition and is uncommon in children.
3. Femoral: Rare in children.

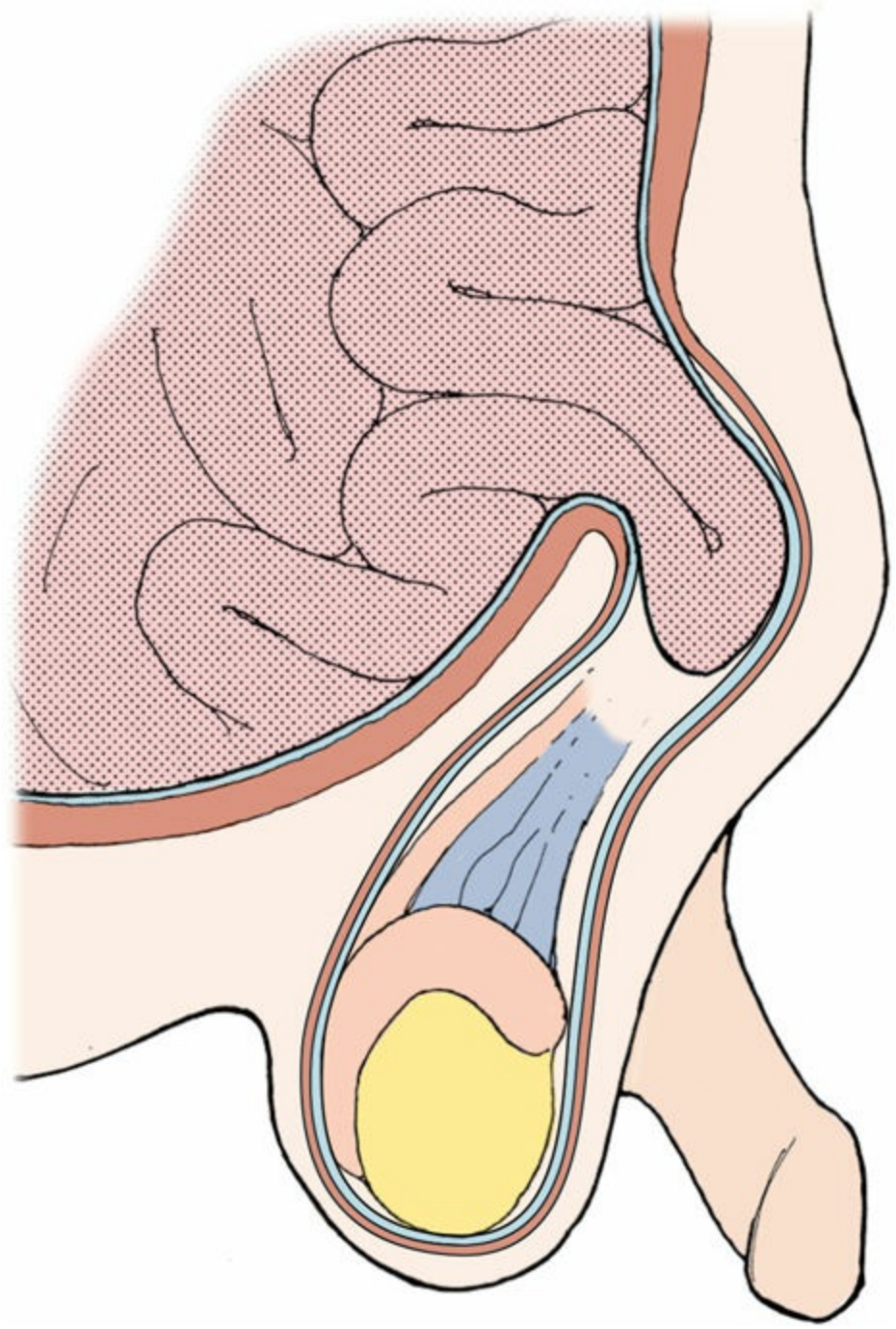

Fig. 5-2 Hernia.

II. EMBRYOLOGY OF INDIRECT INGUINAL HERNIAS AND HYDROCELES

A. During the third month of gestation, the peritoneal lining of the abdominal cavity protrudes out of the internal inguinal ring following the gubernaculum, which attaches

to the base of the scrotum (or, in girls, to the labia major). This is the processus vaginalis. Late in gestation, the testis descends along the same path from the retroperitoneal space through the inguinal canal just posterior to the processus vaginalis and into the scrotum.

B. At approximately the time of birth, the portion of the processus vaginalis between the peritoneum and the scrotum obliterates separating the residual tunica vaginalis in the scrotum from the peritoneum. If the processus fails to obliterate, it is said to remain patent.

C. For obvious embryologic reasons, premature infants will have a much higher rate of patency of the processus vaginalis. If the patent processus is large enough to allow bowel to enter, there is an indirect inguinal hernia. If the processus is patent but the connection is small, a communicating hydrocele is likely to result when peritoneal fluid enters the inguinal canal. If the processus does obliterate, a noncommunicating hydrocele may result by secretion of fluid into the residual tunica vaginalis. This is usually associated with inflammation in the scrotum.

III. INCIDENCE

A. Approximately 1% to 3% of boys have a hernia.

B. In premature babies, the rate is approximately 3 times as high depending on the degree of prematurity.

C. About 10% of children with hernias will have a family history of hernia although there is no known inheritance pattern or gene identified.

D. At least one-third are diagnosed before 6 months of age.

E. The M/F ratio is 8/1. The R/L ratio is 2/1 and about 16% are bilateral, more common in younger patients.

IV. DIAGNOSIS

A. The diagnosis is made, in most cases, by observation, often by the parents. A lump or bulge will be present in

the groin, scrotum, or labia. The lesion is noted particularly at times of increased intra-abdominal pressure (e.g., crying or straining). Generally, the lump will disappear soon after the intra-abdominal pressure returns to normal. In older children, the enlargement may be progressive during the day and recede during naps or at night. When present, the diagnosis is clear-cut. On occasion, the lesion is reported by the parents but cannot be demonstrated in the office, even when the child is crying or straining. Sometimes, the examiner can elicit a "silk glove" sign, in which the layers of the processus vaginalis can be felt around the spermatic cord feeling like "silk rubbing on silk" in the absence of a lump. Alternatively, the parents can bring in a photograph to document it or, if the parents are good historians, repair can be based on history alone.

B. Because hydroceles in the first year of life do not require surgical intervention, it is important to differentiate them from hernias. Most often the physical examination is clear-cut with bowel clearly palpable as distinct from fluid. Sometimes, bowel sounds can be heard in the sac. Transillumination is of limited value in that both hydrocele fluid and bowel fluid/air will transmit light. Bowel fluid/stool, however, will not transilluminate. Needle aspiration is dangerous for obvious reasons. In rare circumstances, a plain abdominal x-ray or an ultrasound will be useful.

C. When there is an obvious lesion, an attempt should be made to reduce the hernia/hydrocele by keeping the child calm and applying gentle pressure on the lump. Bowel will most often be reduced easily. When the sac is filled with fluid, this may also reduce easily. An interesting circumstance occurs when there is a large hydrocele noted in the scrotum that does not reduce easily. Although there is some pressure to repair this because of its obvious appearance, the fact that it does not easily reduce suggests that the connection with the peritoneum is small. In

infants, these may well resolve spontaneously.

D. A special circumstance is the incarcerated hernia. Any child with symptoms of a bowel obstruction (i.e., vomiting and abdominal distention) should be examined carefully for a hernia. In these cases, the mass is usually tender and sometimes there is skin erythema. The hernia may be palpable on rectal examination or confirmed by plain x-ray or ultrasound. An attempt to reduce the hernia should be made as described above. Occasionally sedation with ketamine may be needed as a crying child will make it more difficult to reduce the hernia. If it cannot be reduced, emergent operative intervention is needed. If it can be reduced, the child should be observed closely for signs of bowel injury. Operative repair should be performed soon after.

V. TREATMENT

A. There is no medical management for hernias/hydroceles and the use of trusses is of historical interest only. Hernias will persist indefinitely and will almost always come to repair at some time. Hydroceles may resolve during the first or second year of life and, hence, in most circumstances, a period of observation is justified in most infants.

Hernias in premature infants often will be repaired prior to hospital discharge, but the majority of hernias and communicating hydroceles in children can be repaired as an outpatient surgical procedure with minimal discomfort and morbidity. Surgical repair is performed by ligating the processus vaginalis at the internal inguinal ring, thereby separating the peritoneum from the distal tunica vaginalis. The success rate approaches 99% and the major risk is from the anesthetic. There is some danger of damage to spermatic cord structures as the processus vaginalis is adjacent to them. In normal circumstances, the risk is less than 1%. If surgery on an incarcerated hernia is necessary, the risk is significantly higher, as high

as 6% to 10%, although it is unclear if the damage is related to the repair or the prolonged incarceration, which will reduce testicular blood flow.

B. In infants, at the time of the inguinal hernia repair, it is appropriate to explore the contralateral groin, as approximately 60% will have a contralateral patent processus vaginalis. In older children, the rate of positive exploration is much lower and, hence, in most circumstances, contralateral surgery is not indicated. To be more certain, some authors have recommended direct visualization through the ipsilateral internal ring. The most popular technique has been to insufflate the peritoneum via the processus vaginalis prior to ligation. Crepitus in the contralateral groin indicates a patent processus vaginalis. In addition, a 70-degree lens can be inserted into the processus vaginalis and maneuvered to provide a visual inspection of the contralateral internal ring. If the contralateral ring is open, it is repaired. This procedure is somewhat controversial in that there are no controlled studies to determine if an open ring is associated with a clinically significant hernia/hydrocele in the future. On the other hand, without laparoscopy, at least 2% to 3% of children will present with a contralateral problem that requires surgical intervention.

C. Some institutions have performed minimally invasive repair by a diagnostic laparoscopy via the umbilicus and then passing a needle and suture through a pinpoint incision over the internal ring. The needle is maneuvered around the processus vaginalis under direct vision, avoiding the spermatic cord. It is unclear if the efficacy of this procedure is equal to open repair, or if the morbidity of the procedure is less.

VI. SPECIAL CIRCUMSTANCES

A. **Complete Androgen Insensitivity (Testicular Feminization)**

1. Inguinal hernias are uncommon in girls.

Approximately 2% to 3% of girls with hernias will be found to have a testis within the hernia sac. These girls have complete androgen insensitivity (see Chapter 4**)**. They will have completely normal external genitalia, a shallow vaginal cavity, and should still be raised as females.

2. When found in children, it is best to leave the gonads in place at the time of hernia repair. The local multidisciplinary DSD group should be involved and with the family, a decision should be made electively regarding removing the gonads (due to the risk of gonadoblastoma).
3. These girls are usually totally normal except for infertility and the need for hormone replacement, if the gonads are removed. Some will need vaginal dilation when they are pubertal.

B. **Increased Intra-abdominal Pressure**

1. Communicating hydroceles are unlikely to resolve spontaneously in children with increased intra-abdominal fluid.
2. This is seen in children on peritoneal dialysis and those with ventriculoperitoneal shunts.
3. Early surgical repair is indicated. In these cases, there is a high recurrence rate and repair should be performed with particular caution. It is also appropriate to do a contralateral repair in these patients.

C. **Hernia Uteri Inguinale**

1. This is a rare syndrome resulting from the persistence of müllerian structures secondary to the failure of paracrine secretion of anti- müllerian hormone (AMH) or to an AMH receptor defect.
2. Affected males are not ambiguous at birth and generally present later with undescended testes for orchiopexy or with inguinal hernias.
3. Although not absolutely essential, most would recommend removing the residual müllerian

remnants.

D. **Connective Tissue Disorders**

1. Hernias are more common in children with connective tissue disorders. In particular, children with Ehlers-Danlos and Hurler-Hunter syndromes are prone to hernias. Sometimes the children develop the hernias before the diagnosis of the syndrome.

Neonatal Scrotal Masses

I. NEONATAL TORSION

1. Neonatal torsion is the most common type of scrotal mass.
2. It is usually an incidentally discovered non-tender mass, with no scrotal edema on physical examination.
3. It is thought to begin before birth and only rarely is it possible to salvage the testis.
4. Ultrasound is usually diagnostic if there is a question about the diagnosis.
5. Although controversy exists, many examiners will explore through the scrotum, remove the testis if necrotic, and perform a scrotal orchiopexy on the contralateral side, as there is a rare but catastrophic risk of bilateral asynchronous torsion.

II. TESTICULAR TUMORS

A. These are rare and are usually also asymptomatic and discovered on routine physical examination. They are uncommon in newborns, but if present, they are most likely teratomas. They are of mixed embryologic origin and usually have calcified areas on ultrasound. In addition, they generally do not occupy the entire testis (differentiating them from torsion on ultrasound). In children, they are virtually always benign and excision is generally curative. Partial orchiectomy/enucleation is adequate treatment when feasible based on the anatomy.

B. Also possible is an endodermal sinus (yolk sac) tumor. This is a more serious lesion, in that it may metastasize. It tends to occur in older children. These tumors make α-feto protein (AFP); however, in newborns, the levels of AFP are already elevated, so measuring levels may not be useful, except for comparisons with later measurement. These tumors are amenable to retroperitoneal lymph node dissection, chemotherapy, and radiation therapy when needed, but in most cases, radical orchiectomy and confirmation that the tumor has not spread (CT scan for staging) is all that is needed.

RECOMMENDED READING

Kogan BA. Communicating hydrocele/hernia repair in children. *BJU Int* 2007;100:703–714.

Palmer LS, Palmer JS. Inguinal hernia and communicating hydrocele. In: Wein AJ, ed. *Campbell Walsh Urology*. Philadelphia, PA:Elsevier; 2015.

6 Urinary Tract Infections in Children

Hillary L. Copp, Angelique M. Champeau, and Nicholas M. Holmes

I. INTRODUCTION

A. Urinary tract infection (UTI) is an inflammatory process of the urinary tract due to an infectious agent. The spectrum of presentation ranges from mild lower urinary tract symptoms to a febrile and systemic illness. Variation exists in means of diagnosis, evaluation, and management of children with urinary tract infections, from method of collection of the urine specimen to timing and extent of imaging for workup of UTI.

II. EPIDEMIOLOGY

A. About 3.5 % of children will have a UTI each year. Urinary tract infection accounts for up to 1.75 million office visits and 180 million healthcare dollars spent annually in the United States.

B. The prevalence of urinary tract infection varies with age, sex, and race.

   1. Symptomatic infections occur in 1.4 of 1,000 neonates. Overall, UTIs are more common in females, but during the neonatal period (age less than 4 weeks) males are two times more likely to have a UTI compared with females. Circumcision reduces the odds of UTI by 85% in males. From 1 month to 6 months of age the incidence by sex is equal and from 6 to12 months the ratio of UTIs in males to females is 1:4. Subsequently, infections in males decrease

significantly and remain low compared with females. Girls continue to be at risk for UTI with additional peaks in incidence at toilet training and with onset of sexual activity.

2. The incidence of UTI varies by race with Blacks having a much lower rate of UTI compared with Whites, Asians, and Hispanics.

C. Overall, *Escherichia coli* accounts for more than 80% of all urinary tract infections. Uropathogen prevalence varies significantly with sex, although *E. coli* is the most common uropathogen in both sexes (80% of outpatient female UTIs versus 50% of outpatient male UTIs). *Klebsiella*, *Proteus*, and *Enterococcus* are the next most common bacteria with *Pseudomonas aeruginosa* and *Enterobacter* also known to cause UTIs.

III. RISK FACTORS, GENETICS, AND PATHOPHYSIOLOGY

TABLE 6-1 Sex Ratio of Urinary Tract Infections by Age

	Girls	Boys
Neonate	0.4	1.0
1–6 mo	1.5	1.0
6–12 mo	4.0	1.0
1–3 y	10.0	1.0
3–11 y	9.0	1.0
1–16 y	2.0	1.0

A. **Risk Factors**

In addition to specific underlying factors related to the male versus female anatomy (Table 6-1), urinary stasis and retrograde flow of urine are thought to predispose patients to UTI. Children most at risk for recurrent UTI include those with prior UTI, bladder and bowel dysfunction, and congenital anomalies of the kidneys and

urinary tract (CAKUT), especially those with vesicoureteral reflux (VUR) and high-grade hydronephrosis and hydroureteronephrosis.

1. Female anatomic factors
    a. In females, it is thought that bacteria can gain access to the urinary tract more easily than in males due to the perineal location of the urethral orifice and the shorter female urethra.
    b. The normal perineal bacterial flora may enter the urethra. These bacteria are normally washed out with voiding without consequence. However, if there is a disruption of this normal flora (due to vaginitis, illness, stress, medication) the growth can increase and potentially allow access of enough bacteria to the bladder to cause infection.
    c. In sexually active adolescents, vaginal penetration can predispose to infection.
    d. Vaginal voiding can lead to increased moisture in the perineum allowing for bacterial overgrowth. These children will often complain of “smelly” urine and/or underpants.
2. Male anatomic factors
    a. Foreskin: In infants, an intact foreskin increases the incidence of urinary tract infection 10 times compared with males who have been circumcised. The inability to retract the foreskin is a normal physiologic occurrence in newborn males. At birth, only 4% of males have a completely retractable foreskin. Over time, the foreskin will gradually loosen and become retractable via three mechanisms including penile growth, erections, and smegma production. By 3 years of age, 90% of males will have a retractable foreskin and less than 1% will have phimosis by 17 years of age. The prepuce can serve as a reservoir for potentially uropathogenic bacteria. Studies have

demonstrated the P-fimbriated *E. coli* is more adherent to the inner preputial skin

3. Prior UTI: Children with UTI have a recurrence rate of 30% within 1 year of initial UTI. The rate increases to 50% over a 5-year period.
4. Bladder and bowel dysfunction: Bladder and bowel dysfunction (BBD) is the combination of functional constipation and lower urinary tract symptoms. Constipation has been shown to be prevalent in up to 50% of cases of children presenting with bladder dysfunction. The pathophysiology of BBD is unclear. Rectal distention that comes with constipation may have a mass effect on the bladder, which in turn leads to urinary dysfunction. Another plausible theory is that the rectal and urinary sphincters originate from a common neural network, which is dysfunctional. Children with BBD and any grade of VUR have a higher risk of recurrent febrile or symptomatic UTIs compared with children with high-grade VUR alone (56% versus 30%).
5. Congenital anomalies of the kidneys and urinary tract (CAKUT) includes, but is not limited to, vesicoureteral reflux, ureteropelvic junction obstruction, megaureter, ureterocele, posterior urethral valves, hydronephrosis, hydroureteronephrosis, ureterovesical junction obstruction, prune belly syndrome, bladder exstrophy, and neurogenic bladder abnormalities.
    a. Vesicoureteral reflux (VUR): VUR is the retrograde passage of urine from the bladder to the upper urinary tract (ureters and kidneys). Children with VUR have a higher incidence of recurrent UTI, although the exact pathophysiology is unclear. The cycling of urine in the setting of moderate and severe VUR is likely a nidus for infection. Moreover, there is increased risk that cystitis converts to

pyelonephritis in the presence of VUR. Among children with first-time febrile UTI, VUR is present in about 40% of cases. Reflux is related to the muscle backing of the ureter as it enters the bladder wall (Fig. 6-1). Inadequate length of the submucosal muscular backing can lead to VUR. The anatomy of concave (A) and convex (B) renal papillae can also be a risk factor for pyelonephritis, with concave papillae thought to be more susceptible to refluxing urine into the soft tissue in the kidney (Fig. 6-2).

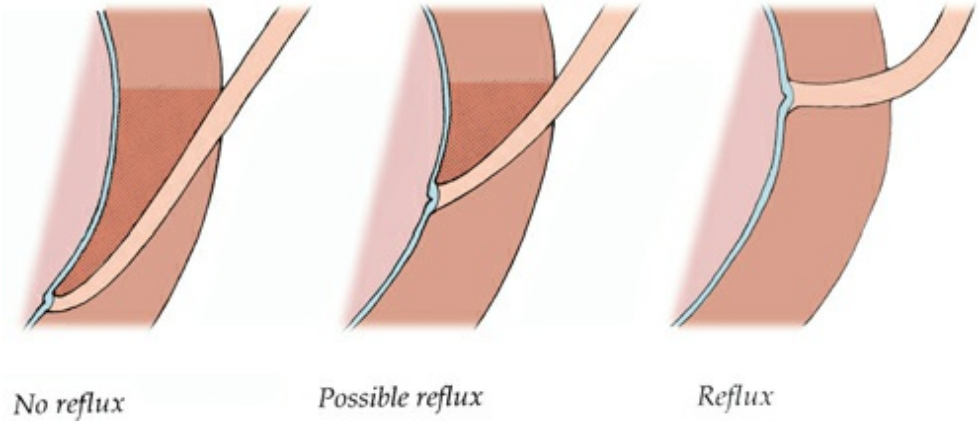

Fig. 6-1 Schematic of the ureter entering the bladder wall. The more extensive the muscle backing the less chance for vesicoureteral reflux.

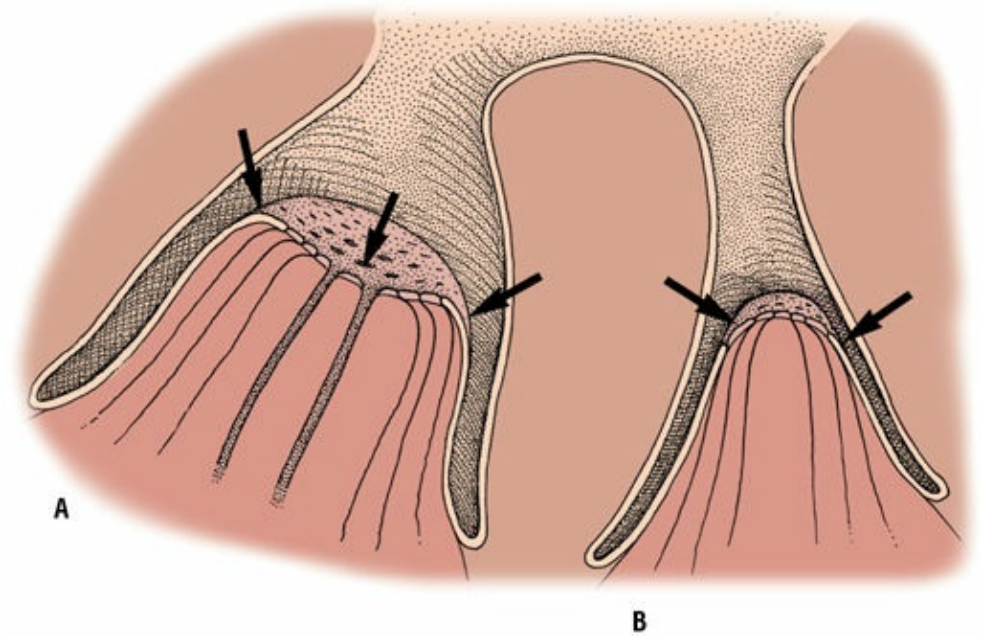

Fig. 6-2 The anatomy of concave renal papillae (A) susceptible to reflux and convex renal papillae (B) protective of reflux.

b. High-grade hydronephrosis and hydroureteronephrosis: Hydronephrosis is a dilation of the collecting system of kidney. Hydronephrosis is now frequently detected during the second- or third-trimester ultrasound screening in up to 3% of pregnancies and is thus termed antenatal hydronephrosis (ANH). Among patients with high-grade hydronephrosis, the UTI rate is reported to be as high as 30% (see Chapters 13 and 14).

c. Neurogenic bladder: Neurogenic bladder can be caused by a variety of diseases but the most common causal disease seen by the pediatric urologist is spina bifida. Many of these patients are managed with clean intermittent catheterization (CIC) or indwelling catheters secondary to poor bladder compliance and risk of damage to their upper tracts. Overall, CIC reduces the risk of UTIs; however, CIC itself can be a nidus for bacteriuria and possible UTI development (see Chapter 11).

d. Kidney transplant registries throughout the world show that one of the most common causes of end-stage renal disease is CAKUT, which includes obstructive and reflux nephropathy. UTIs in the setting of anatomic abnormalities (Fig. 6-1) place the patient at the greatest risk for renal failure. Many patients with hypertension and scarred kidneys have a history of VUR. What is unclear is whether these patients were born with dysplastic kidneys, with a natural history of renal failure, or whether recurrent UTIs caused progressive renal damage.

6. Urologic instrumentation: Catheterization for a procedure such as voiding cystourethrogram and indwelling drainage tubes are known risk factors for UTI (approximately 1%).

B. **Genetics**

1. The etiology of UTI is thought to be multifactorial. There is a higher incidence of UTI among girls with a family history of UTI. The interplay between susceptibility and immune response of the host with virulence of the pathogen is likely an important factor in disease severity.

IV. PRESENTATION

A. The presenting symptoms of UTI are dependent upon the anatomic site of the infection and the age of the patient.

1. Anatomic site of infection

a. An upper tract infection (kidney infection or pyelonephritis) will typically cause general malaise-type symptoms, fever, nausea/vomiting, and/or flank pain.

b. A lower tract infection (bladder infection) will most often present with symptoms such as dysuria, frequency/urgency, or incontinence.

c. It is important to note that although an upper tract infection is assumed when there is a

positive urine culture and a fever, children may have fever with lower tract infections as well. The only way to truly differentiate would be a dimercapto-succinic acid (DMSA) scan at the time of the infection, which is not warranted in most cases.

2. Age
    a. Younger children (infants) will have nonspecific symptoms such as fever, irritability, poor feeding, vomiting, diarrhea, failure to thrive, or jaundice and therefore a certain level of suspicion is required.
    b. Older children will most often complain of dysuria, suprapubic discomfort, frequency, urgency, change in urine odor or color if they have a lower tract infection, and fever and flank pain if they have an upper tract infection.

B. **Asymptomatic Bacteriuria**

It is certainly possible to have bacteria within the urinary tract and be asymptomatic without having clinical infection or renal scarring. The prevalence of asymptomatic bacteriuria has been documented to be approximately 0.9% among young schoolgirls. This does not need to be treated with antibiotics if it is an incidental finding and the patient is asymptomatic. In infants, asymptomatic bacteriuria may be differentiated from true UTI by the absence of pyuria.

V. DIAGNOSIS

A. Once a urinary tract infection is suspected diagnosis is based on examination of the urine. A UTI diagnosis is defined by the combination of pyuria on urinalysis and the presence of at least 50,000 CFU per mL of a single uropathogen.

1. Method of collection
    a. In non–toilet-trained children, a catheterized urine specimen should be obtained. A bagged

urine specimen is only useful if it is negative. If a bag specimen is positive, then a catheterized specimen should be obtained,

b. In toilet-trained children, a clean-catch, mid-stream urine specimen can be obtained after carefully retracting the foreskin and cleaning the glans penis in males and spreading the labia and cleaning the periurethral area in females.

2. Urinalysis
    a. The urine specimen should be checked for leukocyte esterase and urinary nitrite on dipstick or microscopic analysis. In patients who have a negative dipstick and/or microscopic analysis, urine culture is unwarranted and an alternative source of the fever should be sought. However, it should be recognized that a false negative urinalysis result is possible. Specimens for urine culture should be refrigerated if they cannot be sent to the lab within 30 minutes.
3. Urine culture
    a. A positive urine culture is defined by the presence of 50,000 colony forming units per mL of a single urinary pathogen. However, if the urine is collected in a sterile fashion, that is, a catheterized specimen and a single organism is documented by culture, then even if the colony forming units are less than 50,000 CFU per mL, the patient should be considered to have a UTI. In addition, if the symptoms are suspicious of UTI and antibiotics improved those symptoms, a diagnosis of a UTI must be entertained despite a colony count of less than 10^5. Conversely, multiple different organisms or mixed genital flora obtained from a voided specimen should be considered suspicious for contamination even if colony forming units greater than 10^5 are documented. Strict reliance on colony forming

units is unwarranted.

VI. IMAGING

A. Imaging after UTI is controversial (Fig. 6-3). Most often it is not necessary in the acute setting and may be performed in the follow-up.
   1. A renal and bladder ultrasound (RBUS) is recommended after first febrile (temperature greater than 38.5°C) UTI. RBUS always includes evaluation of the kidneys and bladder. It should be noted that the results may be normal despite the presence of other genitourinary abnormalities, specifically VUR. In addition, using RBUS to evaluate children below 5 years of age with a recurrent, nonfebrile UTI to document normal anatomy should be considered.
   2. The indications and timing of voiding cystourethrogram (VCUG) are controversial. The practice parameter of the American Academy of Pediatrics on UTI management in the febrile patient aged 2 to 24 months recommends VCUG after second febrile UTI if the RBUS is normal. Only if there is suspicion of underlying anatomic abnormality on RBUS (e.g., scarring or hydronephrosis or other abnormality) does the practice parameter recommend VCUG after first UTI. In direct contravention, others propose VCUG after first febrile UTI in children 1 to 24 months old due to the fact that up to 40% of children will have VUR. The initial VCUG should always be a *contrast* VCUG and not a *nuclear* VCUG in order to evaluate for congenital anomalies such as ureterocele or posterior urethral valves in males.
   3. DMSA scan may be used to reveal renal inflammation during an acute infectious episode or to assess for scarring from prior infection.

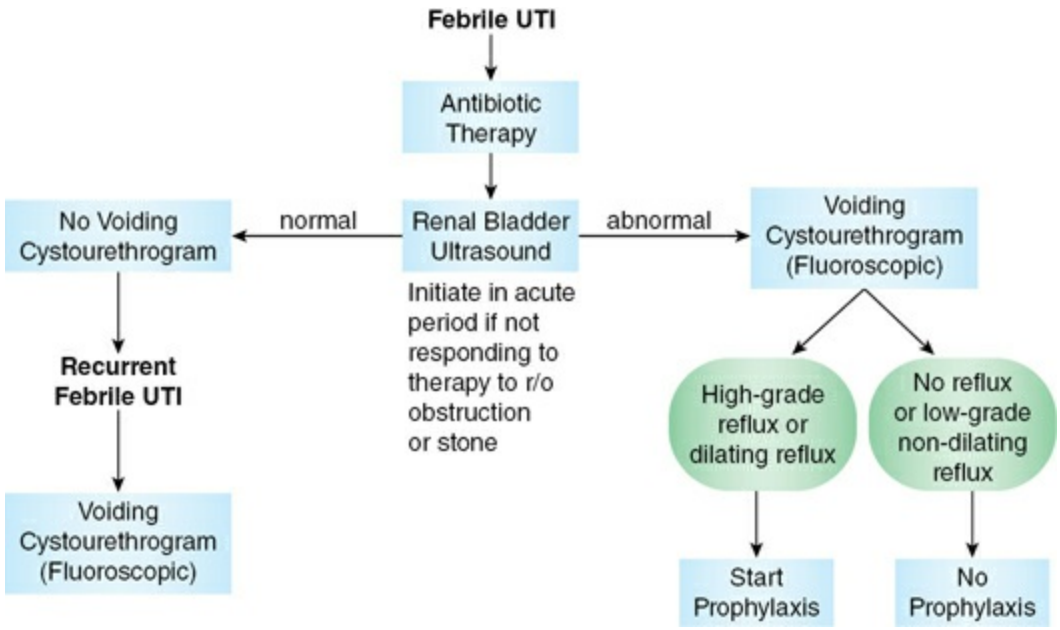

Fig. 6-3 Algorithm for the diagnostic workup for UTI.

VII. TREATMENT

A. Antibiotics

1. The majority of UTIs in nontoxic-appearing children older than 2 months of age may be managed in the outpatient setting as long as compliance with and tolerance of oral antibiotics are not an issue. Overall, less than 1% of patients evaluated in the ambulatory setting for UTI require hospital admission.
2. An antibiotic course of at least 7 days is necessary, as lesser durations have been shown to be inferior. Comorbidities and age of the child are also important factors in the selection and duration of antibiotic therapy. Due to impaired hepatic metabolism, trimethoprim-sulfamethoxazole and nitrofurantoin are not used to treat UTIs in infants less than 2 months of age. Fluoroquinolones are not used as first-line agents, but may be used if necessary based on uropathogen resistance. Nitrofurantoin should not be used to treat febrile UTIs/pyelonephritis as the drug has poor tissue penetration.
3. Empiric therapy based on uropathogen resistance

patterns from published local antibiograms should be initiated if an infection is suspected. Though trimethoprim-sulfamethoxazole is used in approximately 50% of outpatient UTI visits, it is typically a poor empiric choice for pediatric UTI due to high resistance rates. Most uropathogens are susceptible to narrow-spectrum antibiotic agents such as first-generation cephalosporins and nitrofurantoin. Empiric broad-spectrum antibiotic prescription is appropriate in children at risk for resistant UTI such as those with prior UTI history, recent antibiotic exposure, recent hospitalization, and presence of genitourinary anomaly. Broad-spectrum antibiotics include broad-spectrum penicillins (antipseudomonal penicillins and β-lactamase/β-lactam inhibitor combination penicillins), macrolides, fluoroquinolones, second-, third-, or fourth-generation cephalosporins, lincosamides, and carbapenems.

B. **Prevention**

As with many ailments, including urinary tract infections, prevention is the best medicine.

1. Manage bladder and bowel dysfunction.
2. Antibiotic prophylaxis
    a. Several randomized controlled trials (RCTs) have investigated the use of continuous antibiotic prophylaxis (CAP) in the prevention of recurrent UTI in children with VUR. In the RCTs with low risk of bias, CAP reduced the odds of recurrent UTI by half in children with reflux; however, CAP was not associated with decreased rates of renal scarring. Discrepancies in this long-term outcome may be due to the inclusion of children of various ages. Younger children may be more susceptible to the long-term complications of UTI, and/or younger children with VUR may benefit more from CAP.

For this reason, antibiotic prophylaxis for children less than 1 year of age with febrile UTI and any grade of VUR is recommended. For older children who may have less severe consequences from UTI compared with younger children, it may be more prudent to initiate prophylaxis only among those with dilating VUR since fewer people need to be treated to prevent one UTI compared with those with non dilating VUR (NNT for dilating VUR = 14 compared with NNT of 117 for non dilating VUR), the grade of reflux may influence the decision to initiate prophylaxis since the number needed to treat to prevent one recurrent UTI is reduced from 117 in non-dilating VUR (grades I and II) to 14 in dilating VUR (grades III to V). This is common terminology when discussing results from a randomized controlled trial.

b. In children with recurrent infections without congenital anomalies (reflux) in whom bladder and bowel dysfunction have been addressed, prophylaxis may also be warranted (rare).

3. Some patients benefit from prophylaxis only with certain behaviors (sexual activity, change in routine).
4. Although there is an increase in UTIs among neonates who are uncircumcised, justification for circumcision to prevent UTIs among neonates without genitourinary anatomic abnormality is not unwarranted.
5. Although controversial, males who have identified urinary tract anomalies (posterior urethral valves, severe hydronephrosis, hydroureteronephrosis, vesicoureteral reflux) may benefit from neonatal circumcision, thus decreasing the incidence of urinary tract infection.
6. Breastfeeding may confer protection against UTI in the newborn period with secretory immunoglobulin

A (IgA) antibodies and lactoferrin.

7. Probiotics may favorably alter gastrointestinal flora, but data are limited. There are no specific recommendations for their use.
8. No formal recommendations for cranberry-product use to prevent UTI exist, yet there is evidence that cranberry products can be an effective means to lower UTI recurrence. The overall number of recurrent UTIs was reduced with regular drinking of cranberry juice (5 mL cranberry juice per kilogram of body weight, maximum dose of 300 mL per day of Ocean Spray Cranberry Classic, which contained 41 grams cranberry concentrate per 1 liter of juice).

VIII. SPECIAL CIRCUMSTANCES

A. There are many urologic conditions (posterior urethral valves, neurogenic bladders, bladder exstrophy) where clean intermittent catheterization (CIC) is used as an intervention to either preserve renal function or allow for urinary continence. Overall, CIC reduces the risk of UTIs; however, CIC can place these children at further risk for UTI. If these children follow guidelines of frequent and complete emptying with CIC, then infections are typically not common.

B. If the child has had bladder augmentation surgery (see Chapter 11) and is suffering from recurrent infections, then he or she should be instructed on more frequent catheterization and more frequent and efficient bladder irrigation.

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7 Vesicoureteral Reflux

Hillary L. Copp and Laurence S. Baskin

I. INTRODUCTION

Vesicoureteral reflux is defined as the abnormal retrograde flow of urine from the bladder into the upper urinary tract through an incompetent ureterovesical junction. Low pressure reflux without bacterial contamination has not been documented to be harmful; however, reflux in the presence of infection is a risk factor for upper urinary tract infections (pyelonephritis). Untreated upper urinary tract infections have been shown to lead to acquired renal scarring (reflux nephropathy) in children. Congenital abnormalities of renal development may have associated vesicoureteral reflux resulting in a clinical picture of reflux nephropathy but without a history of urinary tract infection.

A. Reflux Nephropathy

It is defined as the following clinical triad.

1. Renal scarring
2. Hypertension
3. Vesicoureteral reflux

II. EPIDEMIOLOGY

The prevalence of reflux varies with several demographic factors of the patient population. Reflux may occur as an isolated entity or with other associated anomalies of the genitourinary tract.

A. History of Urinary Tract Infection

In children without urologic symptoms or history of infection, the incidence of reflux is likely less than 1%. In children with a history of symptomatic urinary tract infection, the incidence of reflux has been estimated to range from 20% to 50%.

B. **Age**

The prevalence of reflux correlates inversely with the age of the study population. With linear growth, spontaneous resolution of reflux occurs in many patients.

C. **Race**

Reflux is more commonly a disease of fair-skinned children. The prevalence of reflux appears to be significantly lower in black children and children of Mediterranean origin when compared to white children. The prevalence of reflux in black children with a history of urinary tract infection is estimated to be approximately 25% of the incidence in the white children population.

D. **Sibling Predisposition**

Siblings of patients with known reflux have approximately a 30% prevalence of reflux, with younger siblings being at greatest risk. A voiding cystourethrogram (VCUG) is recommended if the sibling of a child with VUR has abnormalities on screening renal and bladder ultrasound (RBUS) or has had a UTI.

E. **Sex**

Due to the epidemiology of urinary tract infection in children, boys and girls may present with reflux at different ages. Since urinary tract infections are more common in uncircumcised boys than girls during the neonatal period, many boys will be diagnosed with reflux in the neonatal period. However, after the first year of life, the incidence of urinary infections is much higher in girls than boys. Therefore most school-aged children diagnosed with reflux are girls.

F. **Associated Anomalies**

Although vesicoureteral reflux may occur as an isolated entity, reflux may also occur with other genitourinary

abnormalities.

1. Posterior urethral valves: Congenital bladder outlet obstruction has been associated with reflux in up to 50% of patients. This would be considered secondary reflux.
2. Duplicated collecting system: Reflux is commonly associated with the lower pole moiety of a duplicated system.
3. Prune belly (Eagle-Barrett) syndrome.
4. Bladder exstrophy.
5. Severe voiding dysfunction.
6. Neurogenic bladder.
7. Ureterocele.

III. CLASSIFICATION OF REFLUX

A. **Primary Reflux**

Primary reflux occurs as a result of a congenital deficiency in the formation of the ureterovesical junction in the absence of any other predisposing pathology. Accordingly, these patients may have a laterally ectopic ureteral orifice consistent with a deficient submucosal ureteral tunnel. The majority of otherwise healthy children who present with symptomatic urinary tract infection will fall into the category of primary reflux. It should be noted that the majority of the current guidelines, which have been developed to treat children with reflux, apply mainly to those patients with primary reflux.

B. **Secondary Reflux**

Secondary reflux occurs as a result of other urinary tract anomalies that secondarily cause a decompensation of a normally formed ureterovesical junction. Although secondary reflux may have many different underlying etiologies, the successful treatment of these patients ultimately depends upon the management of the underlying causes.

1. Neurogenic bladder

a. Myelomeningocele
b. Spinal cord injury or lesion
c. Anorectal abnormalities (imperforate anus)

2. Obstruction
   a. Voiding dysfunction
   b. Posterior urethral valves
   c. Ectopic ureteroceles
3. Infection: Cystitis may also predispose an otherwise marginally competent ureterovesical junction (UVJ) to demonstrate reflux.
4. Bladder and bowel dysfunction: The combination of functional constipation and lower urinary tract symptoms is called bladder and bowel dysfunction (BBD). The pathophysiology of BBD is unclear. Rectal distention that comes with constipation may have a mass effect on the bladder, which in turn leads to urinary dysfunction. Others believe that the rectal and urinary sphincters originate from a common neural network, which is dysfunctional. BBD may also predispose an otherwise marginally competent UVJ to demonstrate reflux (see Chapter 6).

IV. GRADING OF REFLUX

Grading of the degree of reflux is important to the management and ultimate prognosis of the patients with primary reflux. More severe grades of reflux are associated with lower rates of spontaneous resolution and a higher incidence of renal scarring. According to the international system, grading of reflux is dependent upon the severity of calyceal changes, ureteral dilation, and redundancy that occur secondary to reflux (see Table 7-1, Fig. 7-1).

TABLE 7-1 Grading of Vesicoureteral Reflux

Grade I: Appearance of contrast in the ureter only
Grade II: Appearance of contrast in the ureter and renal

pelvis without associated dilation or blunting of calyces

Grade III: Mild calyceal dilation without ureteral tortuosity

Grade IV: Moderate calyceal dilation and blunting without ureteral tortuosity

Grade V: Severe calyceal dilation with ureteral tortuosity

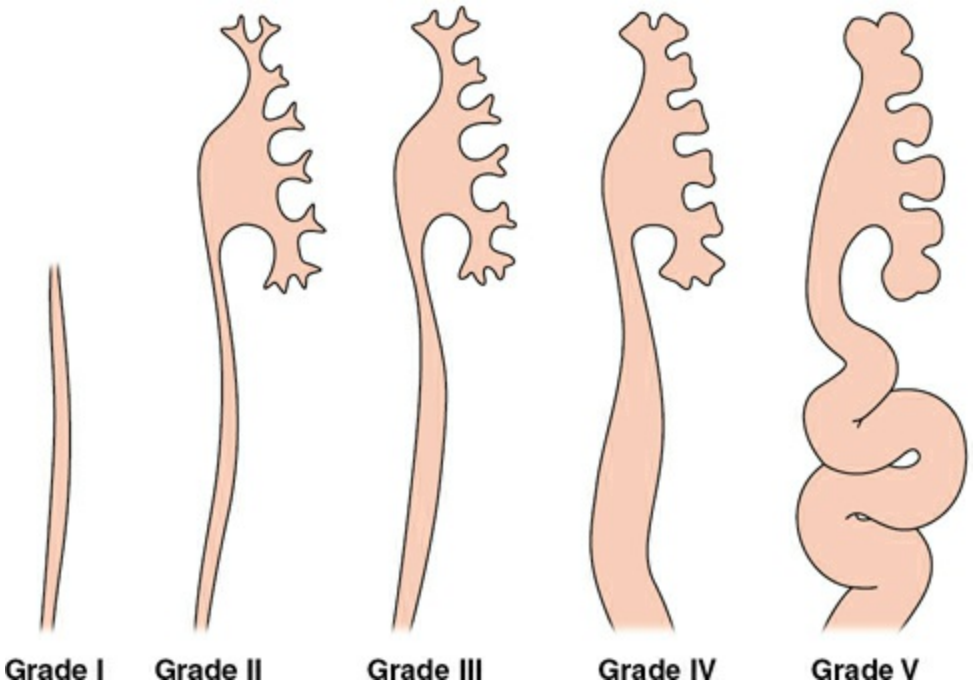

Fig. 7-1 International reflux classification.

V. CLINICAL PRESENTATION

A. **Urinary Tract Infection**

Most children with reflux initially present with an episode of urinary tract infection. Pyelonephritis is the initial presentation in most cases.

B. **Unexplained Febrile Illness**

Other patients may have no documented history of urinary tract infection, but may instead have a history of frequent recurrent illness with unexplained fevers. Some children with reflux and pyelonephritis are mistakenly treated for presumed recurrent otitis. It is therefore of utmost importance to evaluate all children with unexplained fever with the appropriate urine testing (urinalysis and urine culture, if indicated).

C. **Associated Genitourinary Anomalies**

As previously mentioned, reflux commonly occurs associated with other urologic abnormalities. The finding of any of the previously mentioned conditions should prompt consideration for an investigation for reflux.

D. **Prenatal Diagnosis**

Due to the widespread use of prenatal ultrasound screening, fetal hydronephrosis is often detected in utero. Although fetal hydronephrosis can be due to any number of pathologic or physiologic causes (see Chapter 13), infants with prenatally diagnosed, high-grade hydronephrosis (SFU grades 3–4) should be placed on antibiotic prophylaxis until a cystographic examination is performed to either confirm or exclude VUR.

VI. DIAGNOSIS

Imaging following UTI is controversial. Imaging may be done at follow-up and is not usually necessary in the setting of acute infection.

A. **Renal and Bladder Ultrasound (RBUS)**

RBUS is the most commonly used imaging modality to evaluate the urinary tract in children. It is noninvasive, inexpensive, and does not expose the patient to ionizing radiation. RBUS is useful for identification of conditions such as renal duplication, scarring, and dilation of the genitourinary tract. Children less than 5 years of age should have a RBUS performed after first documented febrile UTI or with a recurrent, nonfebrile UTI. As an adjunctive technique, ultrasound can be useful in the grading of hydronephrosis (see Chapter 13), and as a baseline for follow-up studies to monitor renal growth.

B. **Voiding Cystourethrogram (VCUG)**

Vesicoureteral reflux is a radiographic diagnosis. The gold standard study is the contrast voiding cystourethrogram (VCUG). VCUG allows accurate diagnosis and grading of the severity of reflux. VCUG is

recommended after first febrile UTI if there is an abnormality detected by RBUS (e.g., renal size discrepancy, scarring, or hydronephrosis) or after second febrile UTI. However, it should be noted that RBUS is an unreliable modality for predicting VUR and will often be normal despite the presence of VUR.

C. **Urodynamic Evaluation**

Many children with reflux also have voiding dysfunction. Often the diagnosis is suspected by a history of incontinence, frequency, or urgency. If indicated, urodynamic evaluation with monitoring of intravesical compliance can be done at the same setting as the VCUG. This information is important in the management of patients with reflux and other abnormalities of the lower urinary tract (e.g., neurogenic bladder). Appropriate management of the voiding dysfunction often results in resolution of reflux.

D. **Nuclear Medicine Renal Scan**

Renal scan using dimercapto-succinic acid (DMSA) is useful in the detection of renal cortical scars. Some centers have employed renal scans to confirm the diagnosis of acute pyelonephritis.

E. **Nuclear Medicine Cystogram**

Nuclear cystogram is useful as a follow-up study in patients with known reflux. It has the advantage of high sensitivity and lower radiation exposure than the standard VCUG. However, due to its inability to accurately grade reflux and detect associated anomalies (spina bifida, ureteroceles, duplicated systems), nuclear cystograms should not be used for the initial evaluation of reflux.

VII. MANAGEMENT

The primary goal in both medical and surgical management of reflux is to prevent development of pyelonephritis, recurrent urinary tract infections, and the formation of renal cortical scarring.

A. **Medical Management of Reflux**

Low dose, continuous antibiotic prophylaxis (CAP) decreases the odds of UTI development in children with reflux; however, evidence is conflicting with regard to CAP and prevention of renal scarring. Discrepancies in this long-term outcome may be due to study inclusion of children of various ages. Younger children may be more susceptible to the long-term complications of UTI, and/or younger children with VUR may benefit more from CAP. Therefore, antibiotic prophylaxis for children less than 1 year of age with febrile UTI and any grade of VUR is recommended. In the absence of febrile UTI history, CAP is recommended for children with VUR grades III–V who are less than 1 year of age. Similarly, for children older than 1 year, prophylaxis is recommended for higher grades of reflux (grades III–V).

Patients will often have periodic follow-up (yearly to 18 months) to check for the resolution of reflux. The option exists for antibiotic discontinuation without testing for VUR. There is debate as to whether CAP should be discontinued only when VUR has resolved on VCUG versus discontinuation after a certain infection-free interval has been reached. In boys with VUR, the infection rate dramatically drops after 1 year, and, despite continued mild reflux, may be managed conservatively. Because the infection rate remains high after 1 year in girls with VUR, the ideal stopping point is unknown. Often in higher-risk patients CAP is continued through toilet training, as this milestone is frequently associated with UTIs, but once toilet training is completed, the bladder is more mature neurologically and less prone to infection. It is best to avoid testing for reflux during potty training due to the presumed voiding dysfunction during this period.

1. Antibiotic prophylaxis

   There are relatively few effective antibiotic agents available for use in urinary tract prophylaxis in

children. Prophylactic antibiotics are generally given once daily in a dose that is approximately one-half to one-third of the normal therapeutic dose. Table 7-2 lists the commonly used agents and potential serious but rare side effects.

TABLE 7-2 Commonly Used Agents for Urinary Tract Prophylaxis in Children

Agent	Oral Dosage	Precautions
Trimethoprim/ sulfamethoxazole	2 mg/kg PO nightly (Trimethoprim)	Avoid use in the first 2 months due to kernicterus, megaloblastic anemia
Nitrofurantoin	2 mg/kg daily	Pulmonary fibrosis, hemolytic anemia in G6PD deficiency
Amoxicillin	20 mg/kg PO daily	Good choice for first 2 months. Development of resistance common thereafter
Cephalexin	20 mg/kg PO daily	Good choice for first 2 months. Development of resistance common thereafter

2. Treat bladder and bowel dysfunction aggressively (see Chapter 6)
   Patients should be screened for BBD symptoms at

initial evaluation as the presence of unmanaged BBD increases risk of UTI, decreases spontaneous resolution rates of VUR, and lowers surgical cure rates. Children with BBD and any grade of VUR have the highest risk of recurrent febrile or symptomatic UTIs, even when compared with children with high-grade VUR (56% versus 30%).

3. Anticholinergic therapy
   In patients with uninhibited bladder contractions or poorly compliant bladder (see Chapter 8) and secondary reflux, treatment with anticholinergic medications (e.g., oxybutynin) in addition to antibiotics may allow spontaneous resolution to occur.
4. Office visits and follow-up testing
   Patients on medical management should be under surveillance for urinary tract infections. Routine monitoring of urine is not recommended unless the patient has signs and symptoms of a urinary tract infection. Urine should periodically be monitored (yearly) for protein and the patient checked for hypertension, although in most cases proteinuria and hypertension will not be an issue until well into adulthood. Kidney growth as well as scarring should be monitored with ultrasound (every 1 to 2 years). The critical issue is to keep the urine infection-free while reflux is present thereby decreasing the chance of pyelonephritis and hence new renal scarring.

B. **Surgical Correction of Reflux**

Although many patients with reflux can be managed successfully with antibiotic prophylaxis, surgical correction of reflux is indicated when medical therapy is unsuccessful.

1. Indications for surgery
   a. Recurrent episodes of pyelonephritis on antibiotic prophylaxis
   b. Medical noncompliance

c. Breakthrough infections by resistant organisms
d. Persistence of problematic reflux into puberty

2. Results of surgical correction

In experienced hands, anti-reflux surgery is highly safe and effective. Surgical intervention for VUR by either open or endoscopic methods in the correctly selected patient population may be used with good success and a low complication rate. The theoretical risk of ureteral obstruction and kidney blockage can occur with any surgical approach. For this reason, a RBUS should be obtained 4 to 6 weeks after the surgery and at 1 year.

3. Surgical techniques

a. Open surgery: The goal of surgery is to create a functional valve at the vesicoureteral junction. This is accomplished by mobilization of the ureter and creation of a longer submucosal tunnel (at least a ratio of 3:1 for tunnel length to ureteral diameter) for a stronger muscular backing. Two general approaches are used, intravesical (Fig. 7-2) and extravesical (Fig. 7-3). Open surgical repair has a success rate of approximately 95% and a complication rate of less than 2%.

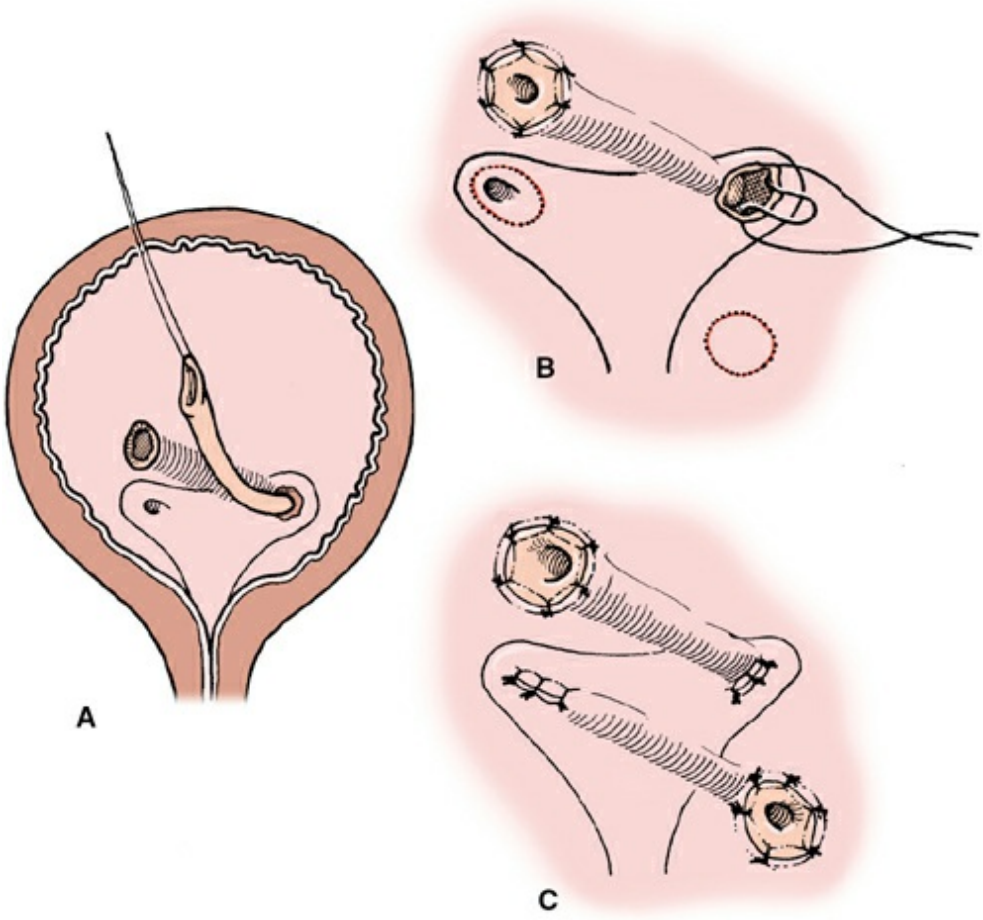

Fig. 7-2 A–C Intravesical ureteral reimplantation technique.

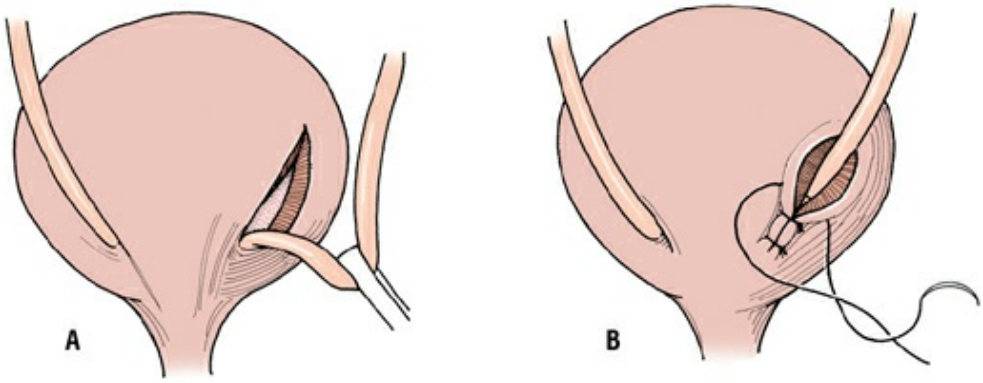

Fig. 7-3 A–B Extravesical ureteral reimplantation technique. Posterior aspect of the bladder (Lich-Gregor procedure).

b. Endoscopic treatment: VUR correction using a bulking agent was initially described in 1981. The most commonly used agent is dextranomer hyaluronic acid copolymer (Deflux). The

procedure is performed by inserting a cystoscope through the urethra into the bladder for injection of the bulking agent. Over time the approach to injection has evolved to the double hydrodistention implantation (double HIT) technique (Fig. 7-4). This technique delivers two intramural injections creating ureteral tunnel and orifice coaptation with improved success rates matching the success of open surgery in some series. Patient selection is an important aspect of procedure success rates, as the rate of cure with endoscopic therapy is less in children with BBD than in those without.

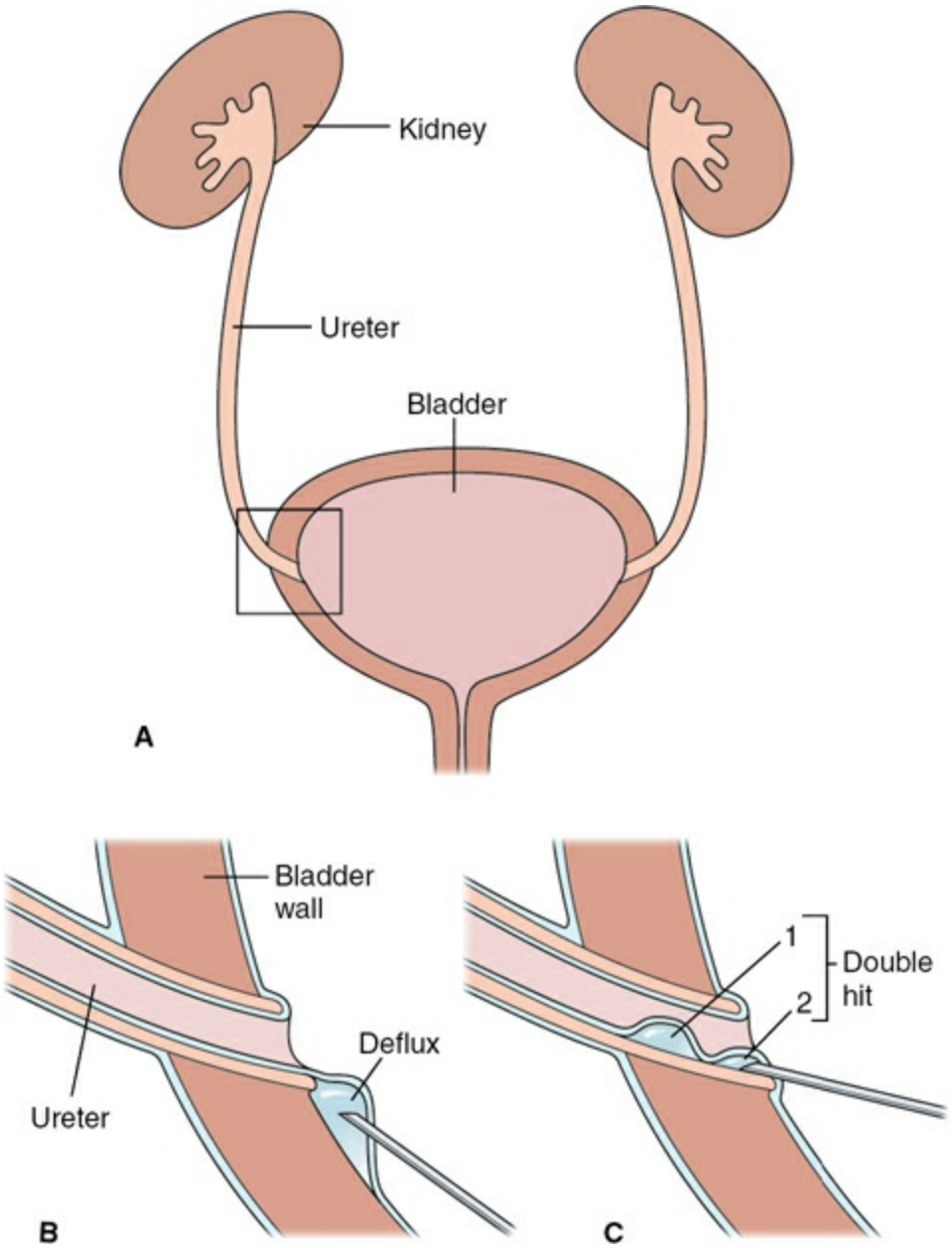

Fig. 7-4 A–C Endoscopic injection of Deflux for the correction of vesicoureteral reflux (double HIT technique).

C. Long-term Follow-up

Long-term follow-up of VUR patients is warranted as patients with a history of VUR are potentially at risk for development of hypertension or chronic kidney disease, especially in the setting of abnormal kidneys by either RBUS or DMSA. Children with a VUR history and an abnormal kidney should undergo annual evaluation

through adolescence, with monitoring of blood pressure for hypertension and urine for proteinuria.

VIII. SUMMARY

Vesicoureteral reflux is one of the most common urologic abnormalities treated by pediatric urologists. An increased understanding of the pathologic mechanisms, bladder and bowel dysfunction, and natural history of reflux has led to improvements in both medical and surgical approaches to treating this disease. The effective treatment of patients with reflux depends upon early detection of reflux and institution of antibiotic prophylaxis in patients at high risk for recurrent UTI and renal damage (patients less than 1 year of age, patients with high-grade VUR, patients diagnosed secondary to febrile UTI, and patients with bladder and bowel dysfunction). Close follow-up and periodic reevaluation are necessary for the majority of patients. When indicated, surgical correction of reflux has been shown to be safe and effective.

RECOMMENDED READING

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8 Daytime Urinary Incontinence/Bladder and Bowel Dysfunction (in the Otherwise Healthy Child)

Angelique M. Champeau

I. INTRODUCTION

A. In order to understand childhood urinary incontinence one must first understand the development of normal bladder control.

1. The neurophysiologic mechanism of normal urinary bladder is controlled by a complex integration of sympathetic, parasympathetic, and somatic innervation that involves the lower urinary tract, the micturition center in the sacral spinal cord, the midbrain, and higher cortical centers. Successful development of normal bladder function requires bladder storage of urine at low pressures with a closed sphincter and complete emptying of the bladder with a voluntary bladder contraction and an involuntary sphincteric relaxation.
2. Starting in the fetus, micturition occurs mainly by reflex voiding at frequent intervals without voluntary control. Bladder filling triggers afferent nerves, which through spinal reflexes cause both relaxation of the external urinary sphincter and detrusor contraction and result in complete emptying of the bladder.
3. By 6 months of age, the bladder capacity increases

and the frequency of micturition decreases.

4. Between the ages of 1 and 2 years, conscious sensation develops.
5. By 2 to 3 years of age, the ability to initiate and inhibit voiding from the cerebral cortex develops. It is at this point that the lower urinary tract is most susceptible to abnormal learned cortical input (this may be as simple as a child who is told not to wet his or her pants).
6. A school-aged child will "normally" void 4 to 9 times per day.
7. Normal bladder capacity (BC) of a child is age related. Age in years + 2 = BC fluid ounces (Age in years + 2) × 30 BC in millimeters.

II. DEFINITION

A. Urinary incontinence is defined as the involuntary leakage of urine in a child older than 5 years of age (the age at which a healthy child in our society should have acquired daytime continence). This particular age, however, depends on the culture of the family. Some cultures expect continence at much younger ages, often due to socioeconomic reasons (lack of availability of diapers and laundering facilities).

B. Causes of urinary incontinence in children can be thought of as acquired (dysfunctional, secondary) or nonacquired (familial, primary). Interestingly, the nonacquired causes of incontinence can lead to acquired (dysfunctional) problems.

III. CLASSIFICATION

A. **Voiding Dysfunction**

1. The term "voiding dysfunction" in childhood means a dysfunction or discoordination of the lower urinary tract without a recognized organic cause (neurologic disease, injury, or congenital malformation).

2. Voiding dysfunction, in general terms, is a discoordination between the bladder muscle and the external sphincter activity (Fig. 8-1) and can take many forms, including inability to voluntarily start or stop voiding, poor bladder emptying, increased bladder capacity, incontinence, and high pressures in the bladder.

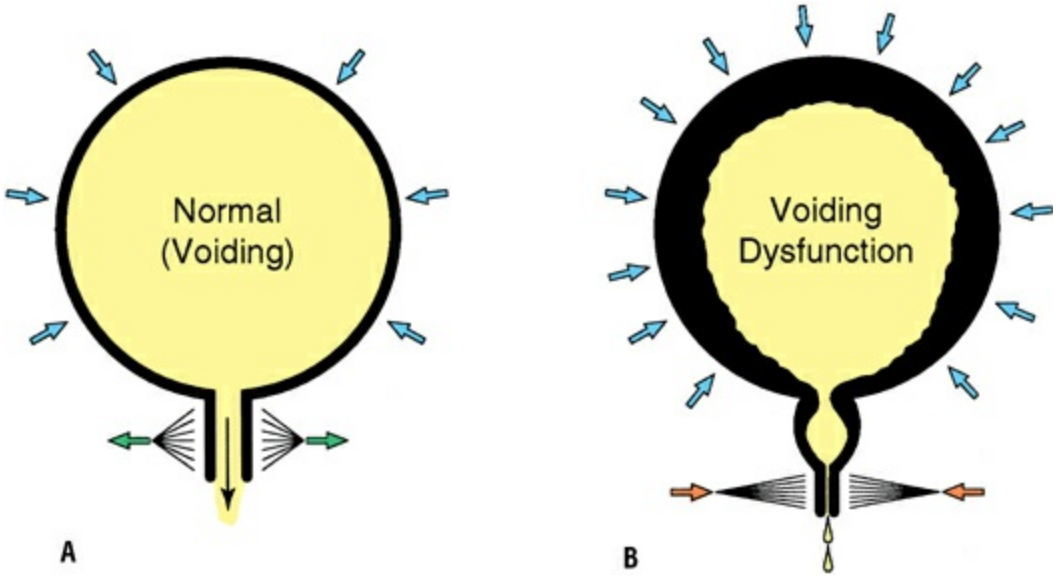


Fig. 8-1 Schematic of normal coordinating voiding (A) and dysfunctional voiding (B).

3. Because older children can control their external sphincter more easily than their bladder muscle, it is easier for them to stop urination than to start it. The contraction of the external sphincter is subconscious and normal during bladder filling but is pathologic during bladder contraction. Although this may be a normal response to an inappropriate bladder contraction, if this continues on a regular basis it will lead to lower and, less often, upper urinary tract deterioration.
4. The contraction of the external sphincter at the time of a bladder contraction has been referred to as pelvic floor dysfunction (PFD). With voiding dysfunction, the PFD is a learned response.

B. **Bowel Bladder Dysfunction (BBD)**
    1. Often, voiding dysfunction is associated with bowel dysfunction: constipation, stool incontinence, and/or recurrent urinary tract infections. When this occurs we classify this as bowel bladder dysfunction (BBD).

C. **Nonneurogenic Neurogenic Bladder (NNNB or Hinman Syndrome)**
    1. Current thinking is that the nonneurogenic neurogenic bladder (Hinman syndrome) is the final clinical result of prolonged severe voiding dysfunction in children without an identifiable neurologic lesion. In this most severe form the abnormal learned voiding pattern can lead to residual urine, hydronephrosis, thickened and trabeculated bladders, vesicoureteral reflux, recurrent pyelonephritis, and ultimately to renal insufficiency. This is most often thought of as an acquired problem but has also been seen in small children prior to the accepted age of normal continence, so there may be a primary problem not yet identified. NNNB is rare.

D. **Vesicovaginal Voiding**
    1. Vaginal voiding can be acquired or nonacquired. The acquired form is very common and often underdiagnosed or considered. Vaginal voiding is caused by children voiding with their legs in complete adduction and results in a portion of voided urine deflecting off the labia and refluxing and pooling in the vagina. This urine slowly dribbles out when the girl stands/walks after voiding. Sometimes the urine will only expel from the vagina when a child coughs or sneezes and will be misdiagnosed as “stress” incontinence (which is not children without neurologic or congenital abnormalities). This problem is more commonly found in obese children, but can be seen in any body habitus. Children with congenital anomalies such as common urogenital sinus anomalies (congenital adrenal hyperplasia)

often have primary vaginal voiding.

E. **Transient Wetting**

1. Transient wetting can occur in association with a bladder infection, illness, or stress (birth or death of family member, sexual abuse).

F. **Uninhibited Bladder or Overactive Bladder (OAB)**

1. The uninhibited bladder can be primary or acquired. A primary uninhibited bladder is also known as a hyper bladder or spastic bladder and can be manifested by incontinence, urgency, and/or frequency. It occurs when the bladder involuntarily contracts (usually prior to age-appropriate capacity). The cause of this is unknown, but it tends to run in families and is often chronic. The hyper bladder will often become more hyper in response to stress or other triggers, not unlike asthma. The younger child may have incontinence at the time of this unexpected contraction while the older child may remain dry but void more frequently than normal. Often, in order to remain continent, children will contract their pelvic floor at the time of the contraction, which can lead to bowel bladder dysfunction thereby exacerbating the original problem. In its acquired form, a child with severe pelvic floor dysfunction can have such high pressures in the bladder that the bladder muscle hypertrophies, which subsequently may cause the bladder to exhibit uninhibited contractions, again exacerbating the original problem.

G. **Voiding Frequency Disorders**

1. Voiding frequency disorders come in two forms, either voiding too frequently or voiding too infrequently. These problems are often self-limited but can be quite frustrating for the child and family. Both may be associated with a psychosocial trigger, but not in all cases can one be identified.
2. Lazy bladder (infrequent voiders): The lazy bladder is a bladder with a large capacity and manifests itself

with very infrequent voiding. The bladder develops poor contractility over time. Usually it is a result of prolonged voiding dysfunction but can also be seen in very young children who void with normal relaxation of the external sphincter albeit infrequent. Children may void as little as 1 to 3 times in 24 hours.

3. Benign urinary frequency: Children with severe urinary frequency syndrome experience an acute onset of extraordinary urinary frequency. They can feel the need to void as often as every 5 to 15 minutes during the day, but most will sleep throughout the night and are dry. Children will usually experience spontaneous remission within 3 months, although temporary recurrence is common.

H. **Giggle Incontinence**

1. Giggle incontinence is a situation in which a normally continent child is incontinent only when laughing/giggling. Interestingly, this same child will *not* become incontinent with other Valsalva maneuvers such as coughing, sneezing, or jumping. True giggle incontinence is rare.

IV. EPIDEMIOLOGY

A. Most otherwise healthy children can manage to stay dry during the day by the age of 4 years.

B. Of all children with a wetting problem, 10% will only have symptoms by day, 75% only by night, and 15% by both day and night.

C. Studies in children just starting school (6 to 7 years of age) have shown that 3.1% of girls and 2.1% of boys had an episode of daytime wetting at least once a week. Most of these children had urinary urgency (82% of girls and 74% of boys). For reasons that are not understood, there is also a difference in prevalence depending if the child lives in colder (2.5%) or hotter areas (1%).

D. **Spontaneous Cure Rate**

1. The spontaneous cure rate for daytime wetting is similar to that for nocturnal enuresis (about 14% of children will improve without treatment each year).

V. ASSOCIATED PROBLEMS

A. **Bacteriuria/Urinary Tract Infection** (see Chapter 6)
   1. There is a strong association between bowel bladder dysfunction and bacteriuria. However, it is not known whether the bacteria cause the bladder dysfunction first or vice versa. Probably both are true and this often leads to a vicious cycle.

B. **Bowel Dysfunction** (see Chapter 10)
   1. Constipation
   2. Encopresis (stool incontinence)

C. **Nocturnal Enuresis**

D. **Psychological Stressors**
   1. Many studies have noted psychiatric disturbances associated with incontinence. However, whether the psychological factor or social pressure is the primary reason for the voiding problem, or if the incontinence leads to the psychosocial problems is difficult to differentiate. Psychosocial or psychiatric help should only be the primary focus in severe cases (e.g., death of family member, sexual abuse).

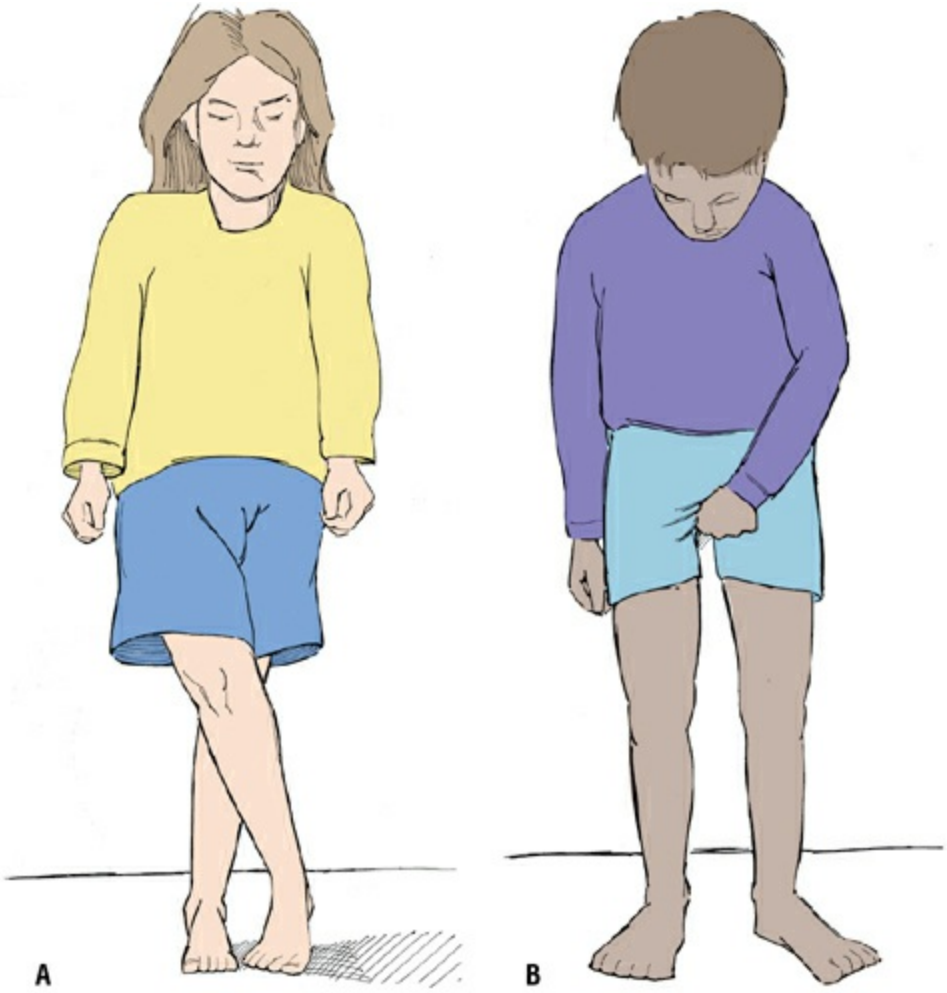
E. **Vesicoureteral Reflux** (see Chapter 7)
   1. Bladder dysfunction may lead to the development, persistence, and when treated, resolution of vesicoureteral reflux. A child with bowel bladder dysfunction may have a functional obstruction and therefore high intravesical pressures during voiding. It is important to recognize the bowel bladder dysfunction in children presenting with reflux, as surgical correction of the reflux will often not change their voiding habits and only part of the problem will be solved.

VI. DIAGNOSIS

A. History

While difficult to elicit in this population, a good voiding history can often lead to diagnosis without further testing. The following are the most common history findings in children with the various causes of incontinence.

1. Voiding dysfunction
    a. The potty dance (Fig. 8-2 A–C): Dancing, squatting, holding, or posturing to avoid leakage. This is thought to be caused by a failure of the cerebral cortex to inhibit a reflex bladder contraction and, in response, either an involuntary void or a guarding sphincteric contraction (helped by squatting) that can temporarily prevent incontinence.
    b. Urinary tract infections
    c. Constipation/encopresis


A
B

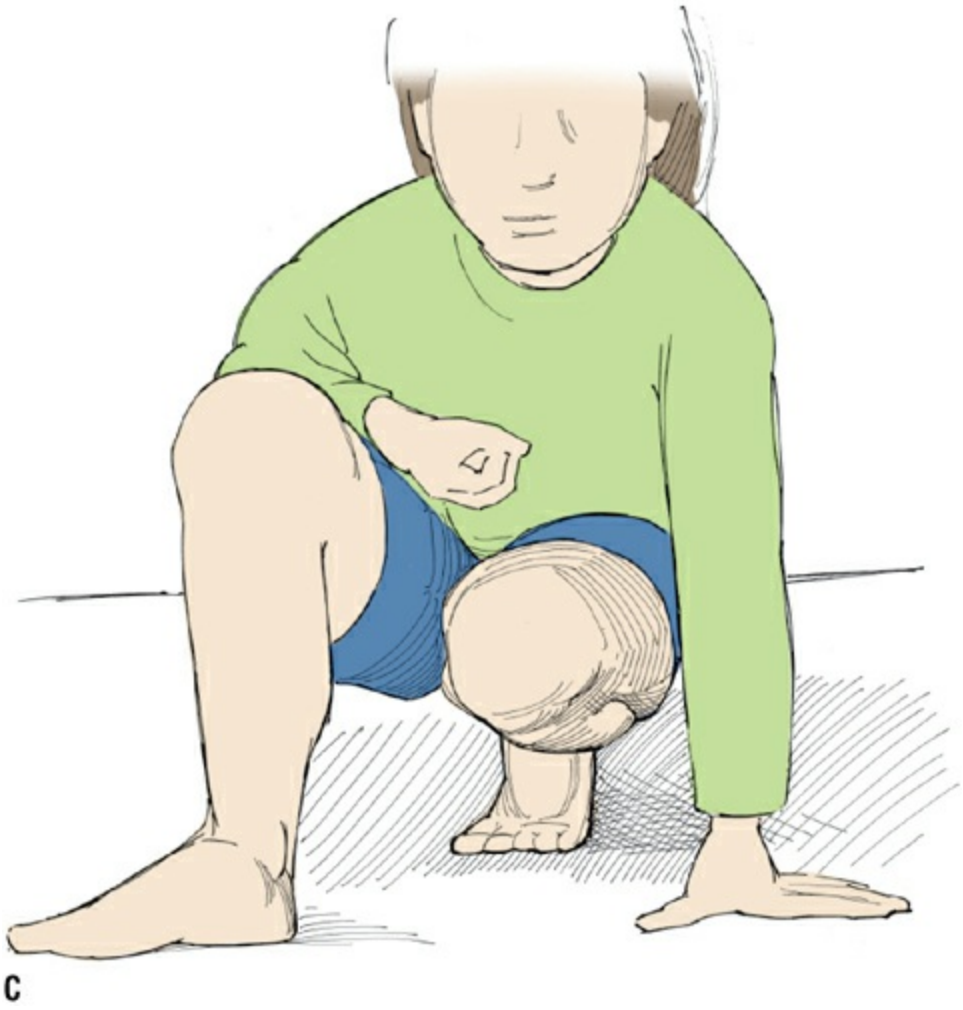


Fig. 8-2 Schematic of various posturing in children with dysfunctional voiding. A: Vincent's curtsy. B: Holding. C: Squatting with heel in perineum.

2. Uninhibited bladder
   a. Frequency
   b. Urgency
   c. Potty dance
3. Frequency disorders
   a. Lazy bladder
      (1) Infrequent voiding (1 to 3 times per day).
      (2) Abdominal straining with voiding.
      (3) Intermittent urinary stream and/or abrupt cessation of urinary stream.
      (4) No sense of needing to void upon waking in the morning.

b. Benign urinary frequency
    (1) Sudden onset of urinating as often as every 5 to 15 minutes.
    (2) Child does not awaken at night.
    (3) Child is continent of urine.

4. Vesicovaginal voiding
    a. Wet after voiding, often described as “leaking.”
5. Giggle incontinence
    a. Only experiences incontinence with giggling, not with other types of Valsalva such as coughing, sneezing, or increased activity.

B. **Physical Examination**

1. General: Self-esteem assessment. Inspection of the underwear for dampness or fecal soiling. Also, the child’s gait should be carefully observed.
2. Abdomen: Pay particular attention to kidneys (hydronephrosis) and bladder and assess for retained stool.
3. Lumbosacral region: Hemangioma, hair patch, asymmetrical dimple, sacral agenesis, or subcutaneous lipoma should be excluded, as these are signs of possible neurological lesions. Observe for muscle weakness with child walking on toes and walking on heels.
4. External genitalia: Anatomy, rash, leakage of urine (at baseline and with straining), perianal sensation, and anal tone. Assess vagina for pooled urine. A rectal exam is very useful but generally not well tolerated. Attention to anomalies (e.g., epispadias, ureteral or urethral ectopy) is important.

C. **Urinalysis**

1. The urinalysis should include measuring specific gravity (to rule out a concentrating defect and therefore high urinary volumes), dipstick for glucose (diabetes and high urinary output), protein, microscopic evaluation, and screening for an infection with a culture.

D. **Voiding Diary**

1. When the voiding pattern cannot be differentiated well by history, some objective measures are needed to document the situation. The most noninvasive (and most useful) of these is the voiding diary (Fig. 8-3). A diary is not only useful for the examining practitioner, but also it will demonstrate the voiding pattern to the child and the family. Almost all urinary incontinence problems can be accurately diagnosed and subsequently treated with a good history, physical examination, and voiding diary (Fig. 8-4).

Day 1

Time:	Amount:	Amount of Wetting in Underwear: Scale: (0-5) 0 = Dry, 5 = Soaked	Comments:

Day 2

Time:	Amount:	Amount of Wetting in Underwear: Scale: (0-5) 0 = Dry, 5 = Soaked	Comments:

Voiding Diary Instructions

1.) Maintain diary for 2 days when a parent/guardian is home with the child (usually a weekend). This does not need to be two days in a row.

2.) If a bowel clean-out was prescribed, wait to start diary at least 2-6 weeks after the clean-out and daily maintenance medicine was started.

3.) The first entry begins when the child wakes in the morning. The child must urinate upon waking.

4.) The child must urinate at least every 2 hours while awake on these days. If they need to urinate more often, that is fine. Please record each urination episode.

5.) Measure each urination episode using appropriate collection device (urinal for boys, and "hat" for girls) and document volume on diary.

6.) Just before each urination episode, assess underpants for wetness. Rate this wetness on a scale of 0 to 5 and document on diary. For example: 0 = Dry, 1 = slight spotting in the underwear, 5 = completely soaked to outside of clothing.

7.) Be sure the child is using proper positioning with urination. For girls, this is sitting with legs widely spread, leaning forward with foot support. For boys, this may be standing, or sitting down.

8.) Use the comment section on the voiding diary to document any issues, and medications. For example: "urinated in the shower, not measured." Or, "Medicine given."

9.) When complete, PLEASE DO NOT FORGET to bring your diary with you to your follow-up appointment at the Pediatric Urology clinic. It is sometimes helpful to fax in or mail in prior to the appointment to be sure it is not forgotten to:
UCSF Benioff
Children's Hopsital
San Francisco and Oakland

Fig. 8-3 A: Voiding diary. B: Voiding instructions.

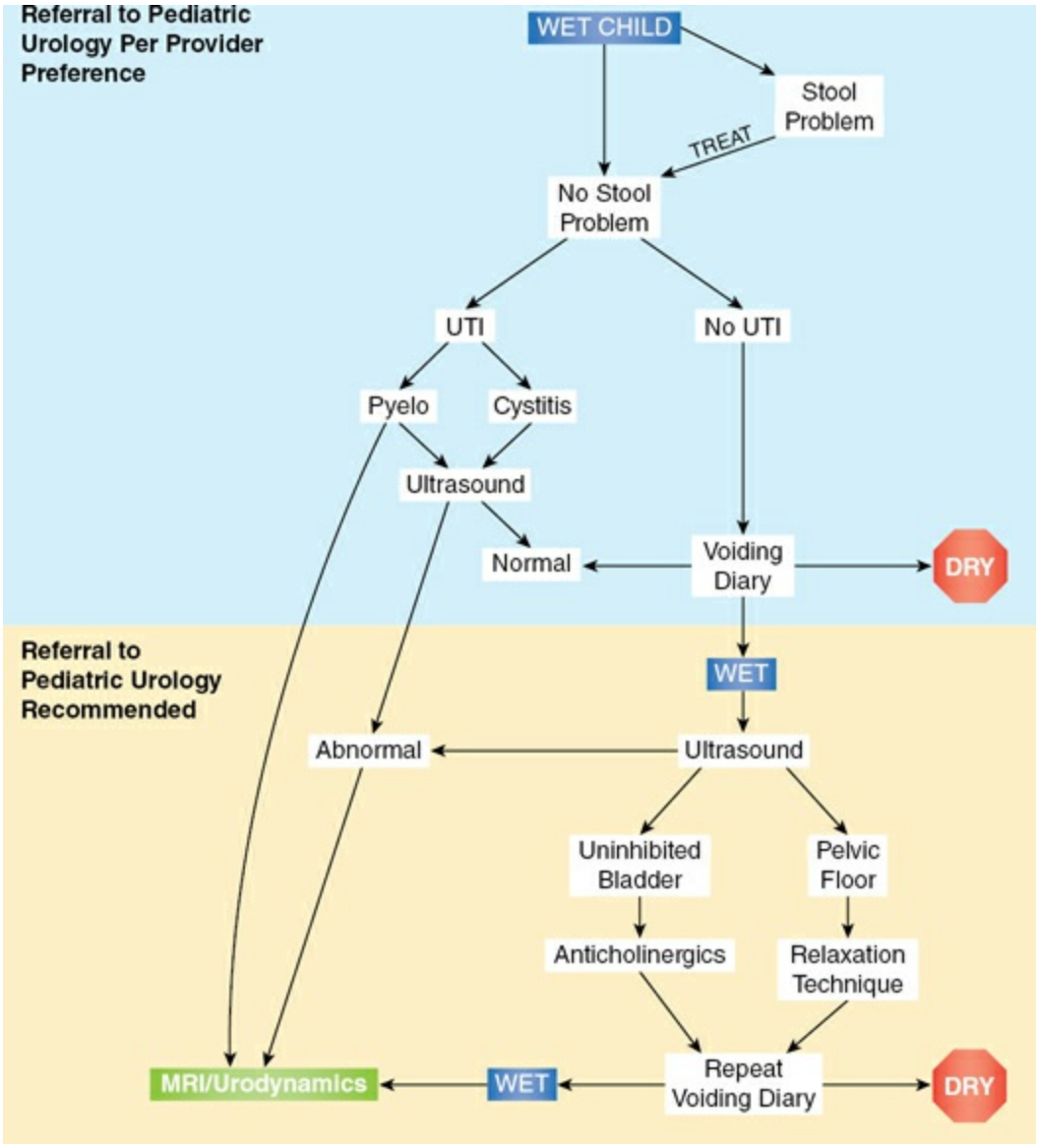


Fig. 8-4 Algorithm for urinary incontinence in the otherwise healthy child.

2. The child should record and document during at least two 24-hour periods the timing and amount of each void as well as the quantity of any incontinence. Correlation and evaluation of the diary can differentiate and recognize many voiding dysfunction problems. It is important to treat any constipation prior to administering the voiding diary.

E. **Urinary Flow Rate**

1. A flow rate is a noninvasive diagnostic tool that can give additional objective information on how a child

empties his or her bladder. This can be done with a machine that gives an objective printout, but can almost as effectively be done by merely observing the child voiding.

a. Staccato voiding: This is another term for an intermittent stream. Usually there will be a delayed start. In contrast to normal voiding, in which there is relaxation of the sphincter, the staccato pattern is caused by bursts of pelvic floor activity during voiding, resulting in bladder pressure peaks and drops in flow rate. Often the bladder will fail to completely empty.
b. Fractionated and incomplete voiding: This micturition pattern is characterized by the use of abdominal straining to help void. The detrusor is hypoactive and therefore abdominal pressure is used to attempt to empty the bladder. Because of the assisted abdominal pressure, the reflex activity of the pelvic floor muscles make the urinary flow very irregular and interrupted, with increases in flow timed with breath-holding (Valsalva cannot be performed while breathing). The flow time is prolonged. It is sometimes difficult to differentiate this pattern in urinary flow from the typical staccato voiding.

F. **Sonogram**

1. If the child has a history of infection, upper tract imaging with sonogram is important. It is important to obtain bladder images postvoiding, to assess residual urine volume in a noninvasive manner. Also a thick-walled bladder can be recognized (more than 5mm). Most children with urinary incontinence will have a normal renal bladder ultrasound; however, obtaining the ultrasound can be very reassuring to the family as well as to the practitioner that nothing more serious is being missed.

G. **X-ray**

1. An x-ray may be obtained to assess for stool retention as history and physical examination are not sufficient.

H. **Voiding Cystourethrogram**

1. This study is reserved for children with a history of febrile UTIs. A voiding cystourethrogram will give information on whether vesicoureteral reflux is present and if residual urine remains after voiding. It will also demonstrate thickened or abnormal bladder musculature. However, when performed as an isolated study, bladder function can be evaluated by inference only. It is important to be sure that the child does not have significant stool retention at the time of testing as it will alter the results.
2. If the morphological and functional correlation with voiding dysfunction and recurrent UTI is appropriate, a video urodynamic study is much more useful.

I. **Video Urodynamic Study**

1. This is an invasive study and is used only in selected cases (e.g., children with complex symptoms, failure of the usual therapy, noncompliance with voiding diaries, or a history of febrile UTIs). The urodynamic study observes the functional phenomenon of bladder filling, sensation, and the voiding process.
2. The cystometry part of the examination requires the placement of a special double lumen bladder catheter, usually transurethrally. For measurement of external sphincter activity, perineal electromyography is the norm and is performed with surface electrodes placed around the anal sphincter. A rectal catheter is placed to subtract any abdominal pressure (crying). The bladder is filled at a moderate rate (1 to 2 ml/kg/min) with a room temperature or warm X-ray contrast fluid (37°C) and the anatomy is characterized simultaneously using fluoroscopy.
3. Studies in children with voiding dysfunction and recurrent UTIs have been able to demonstrate a good

correlation between the presence of unstable detrusor contractions and the clinical symptoms (urge/squatting). Also, if vesicoureteral reflux was present there was a high correlation with very high-pressure unstable detrusor contractions (greater than 70 cm H_2O).

4. It must be remembered that most children with voiding dysfunction will be able to be evaluated by less invasive methods.

J. **Cystoscopy**

1. Cystoscopy, although common in the past, usually with urethral dilation or meatotomy, is now clearly seen as unhelpful, potentially dangerous, and expensive.

K. **Spinal Radiography**

1. If one suspects significant neurogenic bladder dysfunction (spinal defect such as tethered spinal cord), an MRI of the spine (in addition to a full neurologic evaluation) is indicated.

VII. TREATMENT

A. **Treat Constipation**(see Chapter 10)

1. It is imperative to diagnose and treat any constipation prior to moving forward with any treatment of urinary incontinence.

B. After constipation has been treated, the treatment course will depend on the diagnosis, which is usually obtained after reviewing the voiding diary.

C. **Timed Voiding**

1. The most simple and effective form of treatment is “timed voiding.” Because many of these children either do not recognize or ignore the urge to void, a simple program of voiding by the clock at 2-hour intervals can be highly effective. This intervention is beneficial in both uninhibited and lazy bladders (but is easier said than done in the child). It is important to write a note to the child’s school in order for school

staff to set up a timed voiding program while the child is at school. Sadly, many schools use reward systems for *not* using the restroom during class time which can lead to voiding dysfunction and incontinence in children.

D. **Behavior Modification**

1. We recommend reserving behavior modification until after a successful treatment plan has been developed. We do not reward children for being dry, only for following the recommended treatment plan. In the early stages, the children do not understand how to be dry (but they do understand being rewarded for voiding at timed intervals and taking medication). We also do not want to set the child up for failure (rewarding the child for a treatment plan that does not work).

E. **Medication**

1. The use of drugs in the treatment of incontinence is only an adjunct to other bladder treatment regimens. It should be remembered that all medications have side effects and that the physician and parents must reach a collaborative decision that the benefits outweigh the risks. When medications are chosen, it should be emphasized that there is no magic pill, rather they should be combined with other treatments, for example, timed voiding.
2. Anticholinergic medication
    a. This category of medications is used for the uninhibited bladder and will generally have a significant effect.
    b. The most effective anticholinergic drug is oxybutynin. It is both an anticholinergic and antispasmodic agent and has a good safety profile. It is the only anticholinergic that has been studied in children and comes in liquid form. Now it comes in a timed-release tablet, in a gel, and as a patch, all three have a decreased

side effect profile than the immediate release forms in adults.

c. Side effects are common and include dry mouth, constipation, and occasionally drowsiness (often this will resolve after the first week of use). The medication also reduces perspiration and caution should be used in hot climates, where facial flushing is often seen as the first symptom of overheating. Fortunately, most of the side effects are short term and few significant long-term side effects are recognized. Other anticholinergics are available in patients in whom oxybutynin is not feasible. The child and family will decide if the benefit (being dry) is worth the side effects.

d. The above formulations of oxybutynin can be limited in some patients due to their tolerability and efficacy. Developments in elucidating the pathophysiology of OAB and alternative targets for pharmacologic therapy have led to newer agents being developed to manage this condition, including, but not limited to, mirabegron and botulinum toxin. For a review of these newer medications please see the reference. Note that most of these newer medications have not been studied in children.

3. α-Blocker
   a. α-Blockers have been used for children with difficulty relaxing the external sphincter. Studies are limited and this use of α-blockers is considered investigational at this time. Typically timed voiding will be enough for this patient population.
4. Methylphenidate
   a. Methylphenidate has been used to treat giggle incontinence; however, it is investigational and most often the risks of the side effects do not outweigh the benefit. In cases of severe giggle

incontinence causing significant self-esteem issues with social consequences the medication should be considered.

5. Tricyclic antidepressants
    a. Imipramine is used in selected cases, primarily for nocturnal incontinence. It has mild anticholinergic and mild α-adrenergic effects. However, there is no evidence from properly controlled studies that this family of medications is effective in children with dysfunctional voiding. In addition, the high dosage of the medication to obtain anticholinergic effects results in a significant risk of possible toxic side effects (cardiac arrhythmias). It should be used only rarely for voiding dysfunction.
6. Low-dose prophylactic antibiotic medication
    a. If febrile or nonfebrile recurrent UTI or bacteriuria are involved in the problem of dysfunctional voiding, it is advisable to add low-dose prophylactic antibiotic medications. This will remove infection as a cause of voiding dysfunction and allow evaluation of baseline voiding function. One should emphasize to the child and parents that the most important way of eliminating bacteria is frequent voiding.

F. **Biofeedback**
1. Using biofeedback has become quite popular for the treatment of urinary incontinence; however, it is most effective for the pelvic-floor dysfunction cause of incontinence, and in most cases this can be treated with timed voiding alone just as effectively.

G. **Surgery**
1. Surgery is useful only in cases of congenital anomalies (e.g., ectopic ureters or epispadias) or neurogenic findings (tethered cord).

H. **Most Common Treatment Plans for Various Causes of Incontinence**

1. Bowel bladder dysfunction
    a. Treat constipation first.
    b. Timed voiding.
    c. Voiding with relaxation.
    d. Possible prophylactic antibiotics.
    e. Clean intermittent catheterization: Used rarely and only in the most severe (and rare) forms such as nonneurogenic neurogenic bladder (Hinman syndrome).
2. Uninhibited bladder
    a. Timed voiding.
    b. Anticholinergic with frequent reassessment (symptoms will worsen in times of stress but improve at other times; therefore, the child may not always need to be on medication).
3. Transient wetting
    a. In the case of transient wetting, it is best to focus the attention on the primary problem (infection, psychosocial stressor).
4. Vaginal voiding
    a. For younger children, voiding backward or, for older children, voiding with their legs in abduction is curative. The children should watch the urine go into the toilet; this assures the legs are sufficiently far apart. This limits backflow of urine into the vagina.
5. Voiding frequency disorders
    a. Lazy bladder
        (1) Timed voiding. In severe cases, intermittent catheterization, which is usually temporary.
    b. Benign urinary frequency
        (1) Reassurance with close follow-up.
        (2) Usually self-limited after 3 to 6 months.

RECOMMENDED READING

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review of efficacy, tolerability, and quality of life. *Res Rep Urol* 2014;6:1–16.
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9 Nocturnal Enuresis

Anne M. Arnhym

I. INTRODUCTION

Nocturnal enuresis is a common condition that affects children of all ethnic backgrounds. It may result from a single factor or a combination of several factors in a given child. In general, treatment is considered straightforward and largely dependent on the motivation of the family and child.

II. DEFINITION

Nocturnal enuresis is defined as the persistence of inappropriate release of urine at night beyond the age of anticipated control.

A. **Primary and Secondary**
   Primary enuretics have never had a dry period of 6 months or more, whereas children with secondary enuresis have had a dry period of at least this length of time prior to wetting again. Approximately 20% of nocturnal enuretics can be classified as secondary. Concern about secondary enuresis suggests a more extensive workup, but in most cases may be treated similar to primary nocturnal enuresis.

III. INCIDENCE

A. Approximately 15% to 25% of 5-year-old children have nocturnal enuresis.
B. There is a spontaneous cure rate of 15% each year. This suggests that a normal developmental process may simply

be delayed in kids with primary nocturnal enuresis.

C. Approximately 2% to 3% of older adolescents and 1% to 2% of adults have nocturnal enuresis.

D. Nocturnal enuresis is more common in boys than girls (approximately in the ratio 3:2).

IV. ETIOLOGY

Most evidence suggests that the cause of nocturnal enuresis is multifactorial. Possibilities include the following.

A. **Genetic**

There is an increased incidence of nocturnal enuresis in children whose parents also had this condition.

1. Incidence is 77% (both parents); 44% (one parent); and 15% (neither).

B. **Maturational Delay**

Delayed functional maturation of the central nervous system may reduce the child's ability to inhibit bladder emptying at night.

1. The child's bladder fills, but the sensory output resulting from bladder expansion is not perceived, or the message fails to reach the brain. Therefore, the bladder contraction is not inhibited.
2. Functional bladder capacity while sleeping is small in some children with nocturnal enuresis.

C. **Bowel and Bladder Dysfunction (BBD)**

1. Many children with a history of enuresis also present with suboptimal daytime voiding and/or daytime urinary urgency or continence. Stool retention is commonly noted in this population.
2. BBD is often a limiting factor for patients with nocturnal enuresis. Nocturnal enuresis may resolve with treatment of bowel and bladder dysfunction. If not addressed, bedwetting-specific treatment modalities are also less likely effective.

D. **Sleep Disorders**

Most parents of enuretic children report that their children

are deep sleepers. The findings of scientific studies of the sleep patterns of children with and without nocturnal enuresis, however, show wide variations.

E. **Upper Airway Obstruction**

There are conflicting data that surgical relief of airway obstruction by tonsillectomy, adenoidectomy, or both is associated with resolution of nocturnal enuresis.

F. **Psychological Factors**

Nocturnal enuresis was once thought to be a psychological problem. In most cases, psychological problems now appear to be a result of nocturnal enuresis rather than the cause.

G. **Urinary Tract Infection**

Wetting will be the only symptom of urinary tract infection in approximately 1% of children with nocturnal enuresis.

H. **Nocturnal Polyuria**

1. Nonenuretic children concentrate their urine overnight. This is noted by first morning void with a specific gravity above 1.015. There is a higher rate of poor first void urine concentration in some children with nocturnal enuresis.
2. Children without nocturnal enuresis show a circadian rhythm in the release of antidiuretic hormone (ADH) that increases nocturnally and is associated with lower urine outputs at night.
3. Children with nocturnal enuresis have been shown to have lower ADH levels at night, lower urinary osmolality, and higher urine volumes. It remains unclear whether this is primary or secondary to increased daytime salt or fluid intake.
4. Even if pituitary dysfunction is abnormal, this fails to explain why enuretic children do not awaken and void in the toilet.

Summary: The exact etiology of nocturnal enuresis is often unclear. Therapy is most often prescribed without regard to specific etiology.

V. EVALUATION

A. **History**
   1. Documentation
      a. How many wet nights per week?
      b. How many times each night?
      c. Primary or secondary?
   2. Voiding history
      a. Daytime frequency?
      b. Daytime urgency?
      c. Postponing of urination during the day?
   3. Stooling history
      a. How often does the child have a bowel movement?
      b. Are stools soft/skinny or hard/wide?
      c. Any history of skid marks or straining?
   4. General
      a. Family history of nocturnal enuresis?
      b. General medical history?

B. **Physical Examination**
   1. General, including abdominal (palpate for stool, although may not always be palpable).
   2. External genitalia
      a. Wet underwear or rash, suggestive of daytime incontinence.
      b. For girls, bulge or wetness in the introitus may indicate an ectopic ureter.
   3. Neurologic
      a. Spine lesion (palpable sacrum, hemangioma, hairy patch, deep dimple, lipoma).
      b. Gait and movement.

C. **Urinalysis/Urine Culture**
   1. Specific gravity, glucose, protein.
   2. Urine culture if urinary tract infection is suspected.

D. **KUB X-Ray** (to rule out stool retention)
   1. Significant stool retention is often present despite subjective report of regular stooling and no palpable stool on abdominal examination.

E. **Renal/Bladder Ultrasound**
   1. In teenage patients with persistent nocturnal enuresis despite treatment, ultrasound may be reassuring.

F. **Urodynamic Study**
   1. To aid in ruling out neurologic cause of nocturnal enuresis (i.e., tethered cord).
   2. Very rarely indicated or useful in this population.

VI. TREATMENT

A. **Reassurance**

This may be all that is necessary for younger children and families who are particularly concerned about organic disease. Treatment of bedwetting is most effective in children who are motivated to be dry and ready to cooperate with the recommendations.

B. **Lifestyle Adjustments**
   1. Timed voiding: Attempting to void at least 5 times a day without postponing.
   2. Increased hydration during first half of day so less thirsty in the evening.
   3. Reward child for that which they can control (i.e., cooperating with the treatment plan, rather than for being dry, which they cannot control).

C. **Pharmacologic Therapy**
   1. Desmopressin acetate (DDAVP)
      a. Tablets 0.2 to 0.6 mg before bed (intranasal formulation no longer considered safe).
      b. Reduces urine output.
      c. Reduces wet nights in approximately 60% to 70% of kids, high relapse rate.
      d. Danger of hyponatremia (very rare), but *must* limit fluids after dinner.
      e. Good for camps/sleepovers, but may be used with regularity as well.
      f. An option for families wanting potentially faster results, less interested in long-term resolution. Also for families for whom a bedwetting alarm

is not feasible.

g. Few side effects.

2. Oxybutynin (anticholinergic): Not effective unless child is thought to have a small functional bladder at night.
   a. For maximum effect, may be used in conjunction with DDAVP at night.
   b. Recommended dose is 5 to 10 mg at bedtime.
3. Imipramine hydrochloride (antidepressant)
   a. Mechanism of action unclear (altered sleep cycles, mild anticholinergic effect).
   b. For children aged 6 years and below: Initially 10 to 25 mg at bedtime. If inadequate response after 1 week, increase by 25 mg/day. Maximum daily dose: The lesser of 2.5 mg/kg/day or 50 mg/day if 6 to 12 years old; and 75 mg/day if older than 12 years of age.
   c. Success rate is 50% (very high relapse rate when medication is discontinued).
   d. Side effects: Daytime sedation, anxiety, insomnia, dry mouth, nausea, and adverse personality changes.
   e. Overdose can result in fatal cardiac arrhythmias, hypotension, respiratory distress, and convulsion. Tapering of medication is recommended to minimize withdrawal symptoms.
   f. Due to risk of serious side effects, not considered first-line pharmacologic treatment for nocturnal enuresis.

D. **Bedwetting Alarm (Conditioning)** (Fig. 9-1)
1. Alarm attached to underwear that goes off when urine wets the sensor.
2. Works in the school-aged child with a motivated family and child. Most children will sleep through the alarm and *require an adult to wake them from deep sleep!* Child must stay awake for 10 to 15

minutes and remember having done so in the morning. Alarm will gradually go off less and less.

3. Takes 2 months on average.
4. Mechanism of action is unclear (heightened sensation and waking with bladder distention).
5. Difficult for families to use, but the cure rate is greater than 50% to70% when used properly. Retreatment is often successful in relapsing patients.
6. Average alarm system that clips to briefs (pull-up may be worn over brief) costs around $40 online.

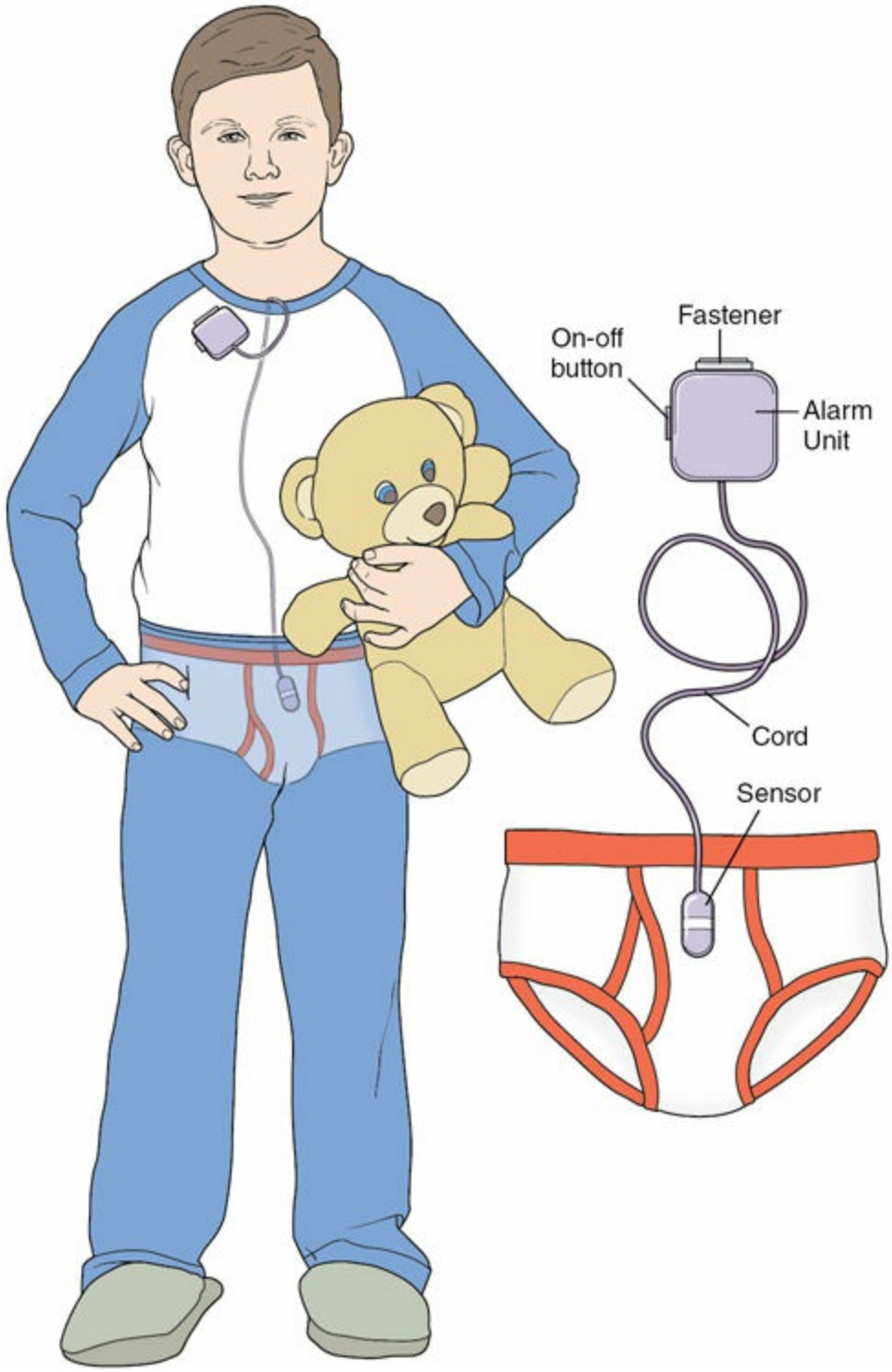

Fig. 9-1 Bedwetting (enuresis) alarm which is activated when a sensor that is placed in the undergarments detects moisture. The arousal is typically an auditory alarm or vibrating pager.

E. Hypnosis

There are conflicting data to support the effectiveness of hypnosis for children who wet the bed. It is a reasonable option for families who desire a non-pharmacologic approach and/or an option aside from the bedwetting alarm.

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10 Constipation and Urologic Conditions

Angelique M. Champeau and Karla M. Giramonti

I. INTRODUCTION

There is a strong correlation between constipation and urologic conditions. Constipation should be considered in the following urological problems.

A. **Urinary Tract Infections**
   1. Approximately one-third of children with recurrent urinary tract infections have associated bowel problems. Infections will recur in most of those whose bowel problems are *not* treated and in far less of those treated.
   2. Approximately 10% of constipated children have recurrent urinary tract infections.

B. **Uninhibited Bladder** (see Chapter 8)
   1. Children with recurrent urinary tract infections and constipation often will have uninhibited bladder contractions. After treatment of the constipation, many will have resolution of the overactive bladder and its associated symptoms (incontinence and recurrent infections).

C. **Vesicoureteral Reflux**
   1. Vesicoureteral reflux is more likely to resolve if concurrent constipation is treated.
   2. Constipated children with vesicoureteral reflux are more likely to have breakthrough urinary tract infections and more likely to have postoperative complications.

D. **Ultrasound Findings**

1. Constipated children can have a significant increase in postvoid residual and upper renal tract dilation compared to children who are not constipated.

E. **Incontinence**
   1. One-third of constipated children will also have daytime urinary incontinence. If constipation is treated, most will have improvement in daytime wetting.
   2. One-third of constipated children will have nighttime urinary incontinence. If constipation is treated, then two-thirds will have resolution of nighttime wetting.

II. DEFINITION

A. Constipation can be defined as hard, small stools, infrequent bowel evacuations, abnormally large stools, difficult or painful defecation, and/or encopresis (smearing).

III. ETIOLOGY

A. The most common cause of constipation in the otherwise healthy child is “withholding” of stool due to toilet training, dirty or public bathrooms, lack of privacy, too busy playing, past painful defecation, changes in routine or diet, and/or intercurrent illness. Some children will experience pain with the large stools and will then hold their stool even longer.

B. The action of withholding stool causes the rectum and colon to expand to accommodate the increasing amount of stool. The stool will increase in size and as the body reabsorbs more water, the stool becomes increasingly hard. As the rectum expands the normal urge to defecate diminishes. As the cycle is repeated, greater amounts of stool are built up in the bowel and motility, rectal elasticity, and sensation further decrease. Subsequently, some children will begin to have encopresis due to looser stool leaking around a rectal impaction or because the

muscles used to withhold become fatigued.

C. No organic etiology is found in 90% to 95% of children with constipation.

IV. PRESENTATION

A. A child will not typically “present” to the urology clinic with a complaint of constipation. These children will more often present with urologic symptoms such as incontinence or recurrent urinary tract infections.

V. INCIDENCE/EPIDEMIOLOGY

A. Constipation accounts for 3% of pediatric outpatient visits and 25% of gastroenterology visits.

B. Encopresis is present in 1.5% of children at school entry.

C. Boys will suffer from encopresis 3 to 6 times more often than girls. This is thought to be because of the standing versus sitting voiding position used by boys during urination. During urination, the pelvic floor muscles relax, and when the pelvic floor muscles relax, stool in the rectum may be expelled. Since boys stand to urinate, when the pelvic muscles relax with voiding, they may soil their underwear.

VI. DIAGNOSIS

A. **History**

1. If an accurate clinical history can be obtained, then the diagnosis of constipation can usually be made by history alone. Unfortunately, an accurate bowel history in the school-aged child is close to impossible to obtain in most cases.
2. Parental history of constipation can be incorrect in up to one-half of children, particularly when the children are out of diapers. Children are also not good historians as to their own bowel/bladder habits and generally have no frame of reference for normal bowel habits.

3. When using voiding diaries to document bladder function/dysfunction, tracking bowel movements is an important adjunct.
4. The Bristol stool score/chart can be helpful for parents/children to describe consistency of stool (Fig. 10-1).

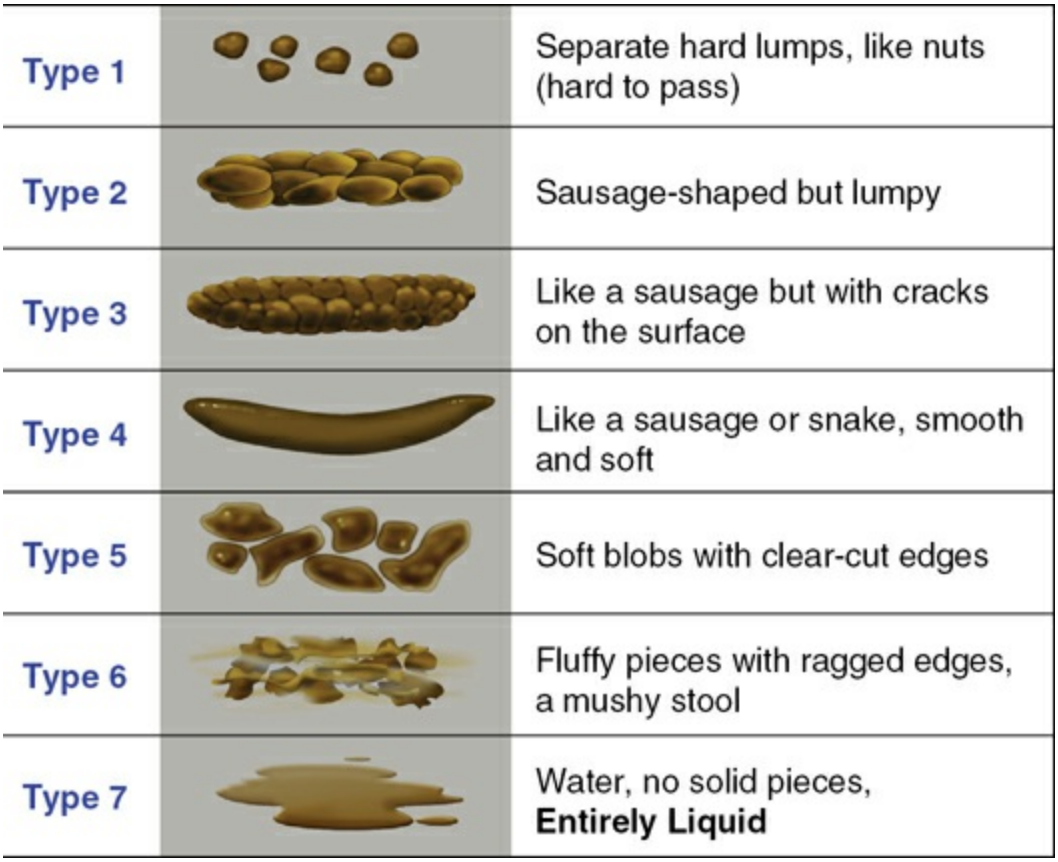
Type 1
Separate hard lumps, like nuts (hard to pass)
Type 2
Sausage-shaped but lumpy
Type 3
Like a sausage but with cracks on the surface
Type 4
Like a sausage or snake, smooth and soft
Type 5
Soft blobs with clear-cut edges
Type 6
Fluffy pieces with ragged edges, a mushy stool
Type 7
Water, no solid pieces, Entirely Liquid

Fig. 10-1 The Bristol stool score/chart helpful for communicating possible constipation.

B. Physical Examination

1. Abdominal examination may reveal hard stool in the abdomen.
2. External examination of the anus and rectum may reveal large amount of stool at the anus.
3. A brief neurologic examination should assess perianal sensation, anal tone, and the presence of anal wink.
4. Although controversial as it can be traumatic for

some children, some clinicians include a formal rectal examination. This can determine the size of the rectum and the amount and consistency of stool.

C. **Radiologic**

1. Abdominal x-ray can further support the suspicion of constipation on history or physical examination. Fecal load can be estimated and objective scoring systems have been developed. An abdominal x-ray is especially useful in children in whom a digital examination can be difficult and/or traumatic.
2. Radiation exposure with x-rays should be considered. Thus, if history is consistent with constipation, treatment can be started without imaging. In children undergoing a VCUG for evaluation of a UTI, the scout film provides an excellent frame of reference.
3. Ultrasound is promising for diagnosis of constipation but guidelines have not been developed at this time.

VII. TREATMENT

Treatment includes two phases: (1) Clean-out to treat constipation; and (2) maintenance for prevention of constipation (Table 10-1).

TABLE 10-1 Medications Commonly Used for Treatment and Prevention of Constipation

Type	Drug	Usual Dose	Possible Side Effect
Lubricants	Mineral oil	<1 year old: not recommended Disimpaction: 15–30 mL/year of age, up to 240 mL daily Maintenance: 1–3 mL/kg/day	Nausea, diarrhea, cramps, vomiting anal itching, possible decrease absorption of fat-soluble vitamins, aspiration
Stimulant	Senna	2–6 years old:	Nausea, diarrhea,

		2.5–7.5 mL/day 6–12 years old: 5–15 mL/day Available as Senokot syrup, 8.8 mg of sennoside/5mL Also available as granules and tablets	cramps, fluid and electrolyte imbalance
Osmotic	Polyethylene glycol 3350 (Miralax)	0.5–0.7 gm/kg daily Max. 17 gm/gay Not FDA approved but readily used	Nausea, stomach fullness, crampin diarrhea, and/or gas
	Lactulose	1–3 mL/kg/day in divided doses Available in 70% solution	Flatulence, abdomina cramps, pain, distention, diarrhea, nausea, vomiting, hypernatremia, perianal itching
	Milk of Magnesia	2–5 years old: 0.4–1.2 gm/day 6–11 years old: 1.2 gm/day >12 years old: 30–60 mL/day	Nausea, diarrhea, cramps, vomiting dehydration, hypermagnesemia hyperphosphatem
	Magnesium citrate	<6 years old: 1–3 mL/kg/day as daily 6–12 years old: 100–150 mL/day	Nausea, diarrhea, cramps, fluid and electrolyte imbalance

	>12 years old: 150–300 mL/day in single or divided doses Available as liquid, 16.17% magnesium

A. **Clean-out Phase**

The goal of the clean-out phase is to literally "clean out" the entire bowel of stool using medications. This will take anywhere from 3 to 7 days depending on the amount of retained stool.

1. Osmotic laxatives
    a. Polyethylene glycol 3350 (Miralax), an osmotic laxative, is first line for the clean-out phase due to its tolerability, effectiveness, and limited side effects. It does not require a prescription and remains safe and effective. Although not yet FDA approved in children, it is considered safe and effective.
    b. Magnesium supplements (magnesium citrate, Milk of Magnesia) are also osmotic laxatives. Available over the counter, inexpensive, and effective, they may be unpleasant to taste and are less effective.
2. Lubricants
    a. Mineral oil is inexpensive and does not require a prescription. Side effects are minimal. It can be made palatable by mixing with ice and fruit or ice cream in a blender. However, a problem with mineral oil is that when used as a clean-out medication, there is a tendency for it to "ooze" from the rectum long after the clean out phase is complete.
3. Stimulants

a. Stimulants (Senna, Ex lax, Ducolax) can also be used in the clean-out phase. Chocolate Ex Lax tastes good, is inexpensive, and quite effective when used along with polyethylene glycol for the severely constipated child. The stimulants are best used only for the short term (clean-out phase).

4. Stool softeners
    a. Stool softeners (Colace) are not generally recommended for childhood constipation. Stool softeners are best used to treat constipation in patients who need to avoid straining (e.g., after surgery).
5. Enemas
    a. Enemas are rarely necessary in the otherwise healthy constipated child (see Section VIII, subsection H: Special Circumstances).

B. **Side Effects**

1. Side effects of all stool medications include soiling, gas, nausea, vomiting, abdominal pain, and diarrhea.

C. **Maintenance Phase**

The goal of the maintenance phase is to “maintain” the empty bowel by having 1 to 2 continent, soft stools per day. This phase will involve medication initially, but the medication is eventually weaned. This phase can take 6 months to 1 year. There are 3 steps in the maintenance phase: medications, diet/fiber, and the daily sit (behavior modification).

1. Medications
    a. Polyethylene glycol 3350: The dose should be titrated to ensure 1 to 2 soft stools per day. As the bowel regains its elasticity and form, over time, the dose should be decreased.
    b. Mineral oil: The smaller doses used in the maintenance phase do not seem to cause soiling or oozing of stool, which occurs when using mineral oil as a clean-out agent. It is important

to have the child take the oil between meals as it decreases reabsorption of fat-soluble vitamins if taken with meals.

c. Lactulose (Enulose): The dose needs to be slowly titrated up until the desired effect is reached (1 to 2 soft stools per day). Starting on "too high" of a dose increases the symptoms of cramping and gas. This medication is available by prescription only.

2. Diet/fiber
   a. Water
      (1) Increased daily intake of water is important and will help soften the stools.
   b. Fiber
      (1) Increased fiber is often recommended in the treatment of constipation; however, there is no direct evidence that increased *dietary* fiber intake is effective in *childhood* constipation.
      (2) Recommended fiber intake is the age of the child plus 5 grams of fiber. Our experience reveals that very few children can take in this much fiber. Therefore, we often recommend a fiber supplement.
      (3) There are many different types of supplemental fiber. For the younger children, the powder form might be the best choice as it can easily be mixed in liquid. For the older child, who can swallow pills, the tablet or capsule form is probably the easiest. For the child somewhere "in-between," perhaps the wafers would be the best choice.
   c. The fluid/fiber ratio is important; not enough fluid with the fiber can make constipation worse.
3. Daily sit
   a. If the child suffers from encopresis then the daily sit is a crucial element of the bowel

maintenance program. The goal is to have the child have a bowel movement at a socially acceptable time, in a socially acceptable place. This is done by sitting on the toilet for 15 to 20 minutes after a meal (due to the normal gastrocolic reflex that stimulates the bowel to move after eating).

b. Children whose feet do not touch the floor should use a stool for support.

c. Positive reinforcement and reward systems improve success. Reward for following the program rather than success, as success takes too much time.

D. **Biofeedback**

Biofeedback and physical therapy can be safe and effective in retraining bowel habits.

VIII. SPECIAL CIRCUMSTANCES

A. **Medications**

Medications that are commonly used to treat the bladder such as anticholinergics often cause or accentuate constipation.

B. **Neurogenic Bowel**

Constipation in the neurologically challenged child is different from constipation in the otherwise healthy child.

1. A neurogenic bowel has a lack of nerve innervation caused by spina bifida, spinal cord lesions, tethered spinal cords, or trauma.
2. The major problems of the neurogenic bowel are constipation and stool incontinence due to the following reasons.
   a. Lack of awareness that the rectum is filled with stool.
   b. Slow motility.
   c. Inability to effectively empty bowel completely.
3. Treatment goals will vary depending on the age of the child and chronicity of constipation.

a. Infants and toddlers (pre–potty training age): Treatment goal in this age group is to prevent constipation. Children who have never experienced long periods of constipation achieve continence later in life with fewer problems than children who have been constipated.
b. Older child (post–potty training age): The goal of the bowel program in the older child is to "wear underwear." Length of treatment will depend greatly on how long the child has been constipated. If the family or child is not ready for the commitment to a bowel program then every effort should be made to at least keep the child free from constipation until the child and family are ready for a continence program.

4. Treatment in the neurologically impaired patient includes the same clean-out and maintenance phases as in the otherwise healthy child with the following additions.
   a. Clean out: Oral medications alone may not be sufficient to clean out the older neurogenic child with severe constipation. Often it is necessary (and more successful) to admit the child to the hospital for a clean out using high-dose osmotic laxative via nasogastric tube. Enemas may be needed also.
   b. Maintenance: The medications and fiber/diet stages of the maintenance phase will be the same as for the otherwise healthy child. However, the daily sit will often not be successful with mere "sitting" on the toilet after a meal. Often it is necessary to add an enema or suppository at the time of the daily sit to assure a positive stool. In general, it is much better to have the neurologically impaired child slightly constipated and focus on emptying the bowels from below using digital stimulation,

suppositories, or enemas to stimulate significant emptying.

c. In severe cases, the Antegrade Continence Enema procedure allows bowel irrigations from above, leading to controlled, excellent emptying with good independence for the child (see Chapter 11, Fig. 11-4).

d. Peristeen

(1) Peristeen is a transanal irrigation system for patients who suffer from fecal incontinence and constipation.

(2) The Peristeen Anal Irrigation System is indicated for use in children as young as 2 years old with neurogenic bowel dysfunction.

(3) Although indicated for neurogenic bowel dysfunction, it has been used in children with significant chronic constipation.

RECOMMENDED READING

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11 Spina Bifida/Neurogenic Bladder

Ronald S. Sutherland

I. INTRODUCTION

Neurogenic bladder dysfunction occurs as a result of developmental anomalies, injuries, and disease of the nervous system. Maldevelopment of the spinal cord, broadly termed as spinal dysraphism and commonly known as spina bifida, leads to myelodysplasia. The most common form is myelomeningocele; other forms are listed in Table 11-1. Myelodysplasia is the most common primary cause of neurogenic bladder dysfunction in children, affecting approximately 1 in 1,000 in the United States. About 95% of children with myelodysplasia have abnormal innervation of the bladder and sphincter. Other causes of neurogenic bladder dysfunction include spinal cord and brain injury and diseases of the central nervous system (CNS) such as Guillain-Barre and CNS tumors. As a consequence of bladder dysfunction these patients are at risk for urinary incontinence, and, more importantly, damage to their kidneys because of increased bladder pressure, vesicoureteral reflux, obstruction, and infection. Early recognition of neurovesical abnormalities enables prompt intervention and usually prevents kidney damage.

Spinal dysraphism arises from a defect in the formation of the neural tube. The etiology is uncertain, but various teratogens such as alcohol and zinc as well as some medications such as valproic acid have been implicated.

Deficient maternal intake of folic acid is well established as a factor leading to development of myelodysplasia, and supplementation reduces the chances of acquiring such birth defects sevenfold.

Injury to and diseases of the CNS cause different forms of bladder dysfunction depending on the location and degree of injury/disease. Two main regions of the CNS are essential for normal bladder function: (1) the pontine micturition complex (upper voiding reflex center); and (2) the sacral spinal cord (lower, or spinal, voiding reflex center). Injuries to the brain (above the pons), to the spinal cord between the pons and the sacral cord, and to the sacral cord and below, produce very different forms of bladder dysfunction. Consequently the management to prevent risks of further complications is different depending on the region injured.

Urologic goals to consider in the care of children with neurogenic bladder dysfunction are: (1) to preserve renal function; (2) to achieve urinary and fecal continence (defined as “out of diapers” at a developmentally appropriate age); and (3) to promote the development of healthy sexual function when age appropriate. By attaining these goals, these patients are much more likely to develop a sense of autonomy and remain healthy.

II. DIAGNOSIS OF MYELODYSPLASIA

A. Prenatal Assessment

1. Serum α-fetoprotein (AFP): Open spina bifida or anencephaly should be suspected if maternal serum α-fetoprotein is elevated more than 3 standard deviations from the norm before 24 weeks’ gestation.
2. Fetal sonography: Fetal sonography and elevated serum AFP combined are highly sensitive (80%) and specific (99%) in diagnosing myelodysplasia.
3. Method of birth: Although vaginal delivery is safe,

some recent studies have suggested that cesarean section may limit neurologic injury.

B. **Newborn Assessment**

After delivery it is important to have a well-trained support staff consisting of, but not limited to, a neonatologist, pediatrician, neurosurgeon, pediatric urologist, orthopedic surgeon, experienced nurses, physical therapists, and social services personnel.

1. Neurosurgical intervention: For open defects such as myelomeningocele where neural elements are exposed, neurosurgical intervention is performed as soon as possible. Abdominal ultrasound (US) is obtained to assess the kidneys. A functional evaluation of the bladder (urodynamic study or UDS) is not usually done before neonatal back closure. If the closure is delayed, however, the UDS can provide useful information. Most children undergoing spinal surgery develop "spinal shock" accompanied by urinary retention for several weeks, so urologic intervention (such as clean intermittent catheterization or CIC) is often necessary before the UDS is done.
2. Evaluate for "occult" spinal dysraphisms: Although open spinal dysraphism is the most common type observed, closed spinal defects (Table 11-1) also occur frequently. Suggestive signs include a sacral "pit" or dimple, a hairy patch, hemangiomas, deformed gluteal cleft, lipoma, and laxity of anal sphincteric tone. Spinal defects are also associated with other conditions including anorectal anomalies, cloacal anomaly, and cloacal exstrophy.

TABLE 11-1 Spinal Dysraphism: Classification and Characteristics

Cystic: Posterior protrusion of spinal elements through spinal defect

Myelomeningocele	Cyst contains meninges, spinal cord and/or nerve roots, and cerebrospinal fluid (CSF)
Meningocele	Cyst contains meninges and CSF
Lipomeningocele	Cyst contains meninges, CSF, and fat
Myeloschisis	Extensive open neural plate or cleft spinal cord
Rachischisis	Complete cleft of vertebral bodies and cord
Noncystic: No protrusion of spinal elements; presence of hair tuft, sinus or dimple, discoloration or lipoma the only sign	
Intradural lipoma	Fatty infiltration of the spinal cord
Diastematomyelia	Bony spicule or fibrous band splitting the cord
Dermoid and epidermoid cyst/sinus	Invagination of surface epidermis
Cauda equina tumor	Cord compression
Anterior sacral meningocele	Anterior herniation of spinal elements into pelvis
Tethered cord	
Primary	Broad, thickened cord preventing upward migration
Secondary	Fixation or compression of cord from postoperative adhesions, fibrous bands, lipoma, and cysts
Syringomyelia	Cystic degeneration of cord

III. CARE OF THE NEWBORN

A. **Evaluation**

1. Urodynamic studies: The goal of UDS is to characterize the compliance and contractility of the bladder and the function of the outlet (the bladder

neck and external sphincter). These tests evaluate bladder pressure during filling (storage) and emptying (cystometry), sphincter activity (electromyography), and radiographic appearance of the lower urinary tract (fluoroscopic cystourethrography). In addition, vesicoureteral reflux may be detected on fluoroscopy during urodynamic assessment. Urodynamic testing is done when the infant can safely be placed in the supine position once the spinal shock phase has passed. Some centers may prefer "watchful waiting" and follow the infant with sonography alone, deferring urodynamic evaluation until hydronephrosis is detected or continence is desired.

2. Sonography: Ultrasound (US) is performed to detect hydronephrosis, which may be the result of vesicoureteral reflux or a "hostile," noncompliant bladder, and to monitor renal growth.
3. Urinalysis and culture: Urinalysis and urine culture should be performed only if the child is symptomatic for a urinary tract infection.

B. **Treatment of the Newborn**

1. Treatment is based upon the urodynamic findings.
    a. Weak sphincter, normal bladder: observation.
    b. Flaccid (arreflexic) bladder: clean intermittent catheterization (CIC).
    c. Hyperreflexic and/or noncompliant bladder: CIC plus anticholinergic medication.
2. Clean intermittent catheterization (CIC): Some centers start all babies on CIC immediately at birth regardless of the UDS findings, although UDS are abnormal in the majority. Eventually most children will require CIC to gain continence or to protect the kidneys, and it is our experience that older children who were started on CIC as infants better tolerate and are more compliant with the CIC than children who begin CIC at a later age. For example, if a baby has a

weak sphincter in infancy, there may no medical reason to catheterize the baby (although one must be certain that the bladder can completely empty). However, later, this same baby will be incontinent and the urologist may operate to "tighten" the sphincter, after which the child will have to do CIC in order to empty the bladder. This type of surgery is usually done close to the age of normal potty training or prior to entry to kindergarten. Unfortunately, the timing of the surgery is at one of the worst stages of development to start a CIC program. The best approach is to educate the parents about the UDS findings, the need for future catheterization, and potential problems they will encounter if they choose to delay CIC so that the parents can make an informed choice.

Early institution of CIC every 3 hours is preferred over the Credé maneuver (suprapubic compression to express urine), which is not physiologic, causes markedly increased bladder pressures, and is not appropriate for long-term management.

3. The addition of anticholinergic medication (see below) in the neonatal period is safe and well tolerated. In the infant who has progressive urinary tract deterioration despite maximal medical therapy, a temporary vesicostomy (surgical diversion of the bladder to the lower abdominal wall) will prove effective.
4. Avoid the use of latex-containing products (see Section V, subsection H).

IV. NEUROLOGIC INJURY AND DISEASE

A. Pathophysiology

1. Brain lesions *above* the pontine micturition center may be caused by trauma, stroke, cerebrovascular accident, and space-occupying tumors. The cerebral cortex can be viewed as having a global inhibitory

effect on bladder function. Without higher cerebral input the bladder develops overactivity, also known as “hyperreflexia” or “spastic” bladder. However, in the acute period after injury or surgery, patients experience CNS “shock” accompanied by flaccidity of the bladder function resulting in urinary retention. After 4 to 6 weeks, the bladder recovers from shock phase and becomes hyperreflexic. Since the two CNS centers for coordinated voiding (pontine micturition center and sacral spinal cord) are intact, coordinated voiding and sphincteric function occur. The patients may be incontinent because of bladder overactivity.

2. Lesions *below* the pons include spinal cord injuries, autoimmune causes, infarction, disk disease, and others. After acute injury, one can expect a period of spinal shock for 4 to 6 weeks with resulting flaccidity, just like with higher lesions. However, once this period is over, expect both bladder hyperreflexia and sphincteric dis-coordination (also known as detrusor-striated sphincter dysfunction or DSSD). Without the inhibitory input of the brain, the bladder becomes overactive, and lacking the coordination by the pontine micturition center, the patient cannot control sphincteric relaxation. These patients are at great risk for elevated bladder pressures and damage to kidneys.

   Patients with spinal cord injury above T1 are at risk for developing autonomic dysreflexia. This is caused by unregulated discharge of sympathetic nerves in response to unrecognized lower stimulation such as bladder overdistension or injury. Patients may develop severe hypertension, headache, sweating, bradycardia, and stroke. Treatment requires removal of the stimulus (empty the bladder) and controlling the life-threatening hypertension.

3. Lesions of the sacral cord occur with trauma or disease in the lumbar vertebra. The terminal end of

the spinal cord, the cauda equina, ends at vertebral level L1–L2. The S2–4 cord is responsible for coordination of voiding function, and the nerve roots from S2–4 emerge at vertebral levels T12–L2.

V. LONG-TERM MANAGEMENT

A. Bladder Function

1. Clean intermittent catheterization (CIC): Early implementation of CIC helps prevent renal deterioration and may preserve some bladder function (decreasing the need for major bladder surgery in the future). Self-catheterization is *not* a sterile procedure, and the vinyl catheters are reusable. Parents and children are taught to clean with soap and water, or dilute alcohol, or peroxide. Catheters are dried and reused for up to a month. Studies show no difference in infection rates between new and reused catheters. Catheters should be upsized to the largest diameter possible for age so that rapid and complete emptying can occur. Most children with myelodysplasia and spinal cord injury do not have normal sensation with catheterization.
2. CIC plus anticholinergic medication: Increased bladder pressure and inadequate capacity may manifest as incontinence, hydronephrosis, urinary tract infection, and suprapubic discomfort. Medical therapy with anticholinergic medication (such as oxybutynin 0.1 mg/kg three times per day), coupled with intermittent catheterization, is usually sufficient to provide both a low bladder pressure and continence. In some children, higher doses may provide additional detrusor relaxation with enhanced continence. If anticholinergic side effects (e.g., facial flushing, blurred vision, dry mouth, constipation) become intolerable, intravesical instillation can be utilized. In older children, a more selective anticholinergic agent, sustained release formulation

such as Detrol LA, or transdermal patches may provide equal efficacy with less side effects.

3. Surgery
    a. Bladder augmentation: When medical therapy fails to achieve adequate low-pressure capacity, surgical enlargement of the bladder may be achieved by intestinal augmentation (Fig. 11-1). Because of the potential for complications, this procedure should be undertaken only when the other options have failed. Surgeons mainly use ileum (20 to 40 cm) because of its proximity to the bladder and blood supply, but other segments including colon and stomach are occasionally used as well. Complications include electrolyte and acid/base derangements (chronic acidosis), chronic mucus production, and problems resulting from open bowel surgery (peritonitis and bowel obstruction). Patents with bladder augmentation also have a higher risk for urinary tract infections and bladder calculi. The use of stomach for augmentation has become rare because of the problem of acid in the urine.

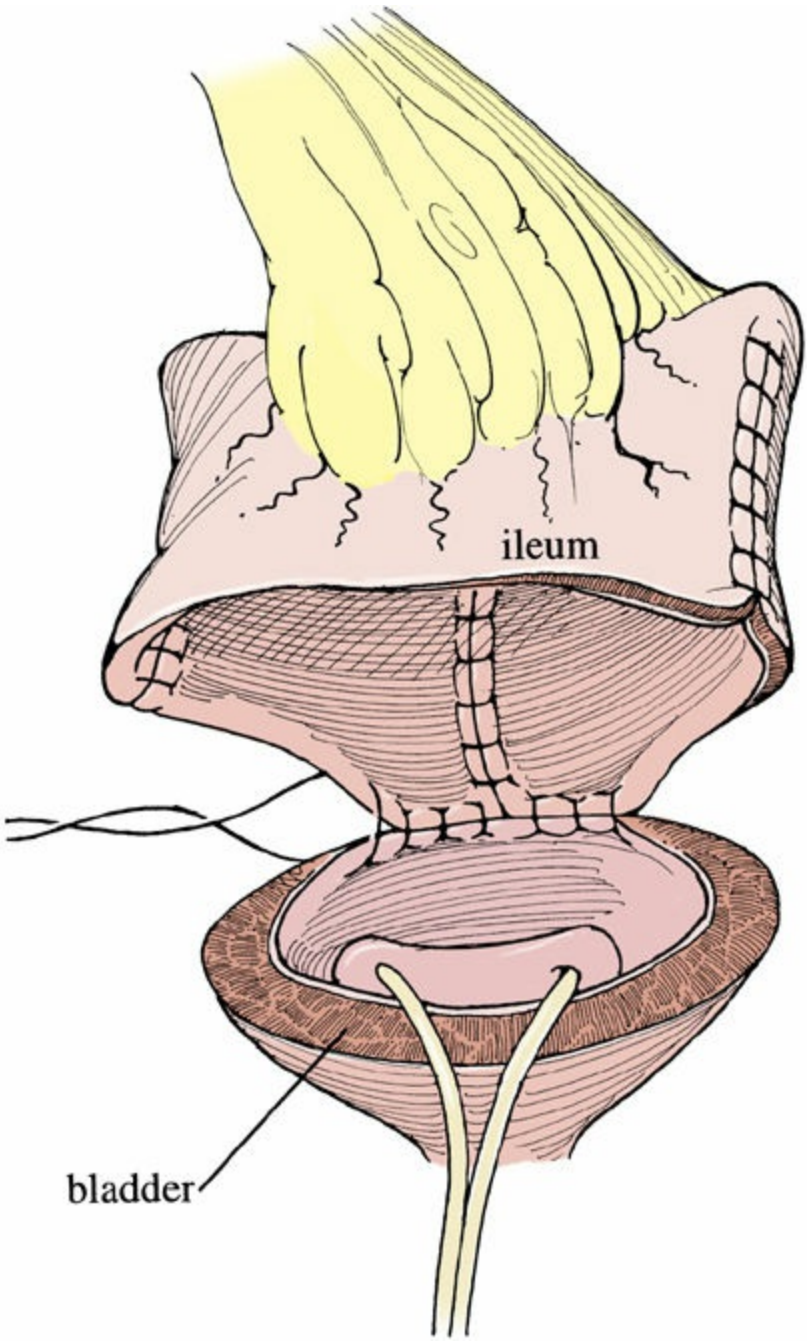

Fig. 11-1 Augmentation of the bladder is performed using a segment of ileum as a patch to increase the capacity and decrease the pressure of the bladder.

b. Endoscopic injection of botox: In order to eliminate the complications associated with enterocystoplasty there have been several proposed surgical alternatives. Ureterocystoplasty (using a dilated ureter),

demucosalized bowel segments, bladder auto-augmentation (creating a low pressure bladder diverticulum), have not been widely adopted. Recently, investigators have been reporting treatment of poor bladder compliance and detrusor overactivity secondary to neuropathic bladder dysfunction, by cystoscopic injection of botulinum toxin A (Botox). The injections are performed as an outpatient procedure or office procedure. Injections need to be repeated every 6 months. Long-term studies are needed to determine if endoscopic injection of Botox at 6-month intervals will avoid and not just delay augmentation cystoplasty.

c. Follow-up of patients after augmentation
   (1) Metabolic evaluation: These patients are at risk for metabolic disturbances due to absorption or secretion of electrolytes and through the bowel segments. With ileum and colon, hyperchloremic metabolic acidosis is most common; with stomach, hypochloremic, hyperkalemic metabolic alkalosis can occur. Chronic acidosis alters calcium metabolism and thus bone development. Therefore, serum electrolytes (including bicarbonate) and calcium, phosphorous, and magnesium levels should be checked annually or as needed.
   (2) Renal function: Assess serum creatinine and electrolytes at least annually.
   (3) Urine microscopy: In children who perform self-catheterization, the urine will most likely be colonized with bacteria and may have a few leukocytes and red blood cells. Moreover, after an augmentation with an intestinal section, the urine will almost always be filled with mucus and bacteria.

Unless the child is symptomatic or has vesicoureteral reflux, this should not be treated with antibiotics.

(4) Continent catheterizable stomas: After augmentation of the urinary bladder, catheterization is nearly always required to facilitate complete drainage. In patients who are wheelchair-bound or those who have severe scoliosis/lordosis, catheterization may be physically challenging. Others may not be able to see or reach the urethra. In these individuals, a catheterizable, continent stoma may be created to provide an easily accessible route of bladder emptying (Fig. 11-2). This may be created from appendix, ileum, or colon. Boys with intact urethral sensation, in whom self-catheterization may not be well tolerated, may also benefit from an abdominal catheterizable stoma.

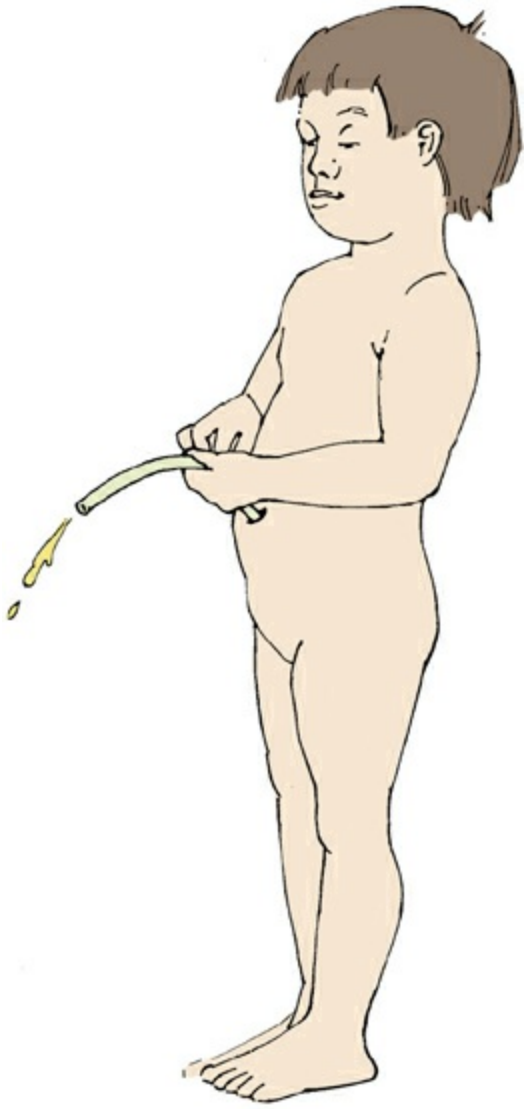

Fig. 11-2 Child inserting a catheter into a continent catheterizable channel from the umbilicus to the bladder.

B. **Continence (Sphincter Function)**

1. Medication: Urinary incontinence that is related to inadequate outlet resistance rather than inadequate storage may be improved by α-adrenergic medication (pseudoephedrine), but most often sphincter function will be improved only by surgical correction.
2. Periurethral injection therapy: Injection of bulking agents such as collagen or Deflux around the bladder neck may result in short-term improvement in continence. The advantage of this technique over

open surgical reconstruction to improve outlet resistance is the minimally invasive nature of this endoscopic procedure. Unfortunately it is only rarely successful in the long term.

3. Bladder neck suspension and reconstruction: Suspension of the bladder neck and proximal urethra to the pubis using sutures or compression by a "sling" of rectus fascia can be coupled with bladder neck reconstruction. Success rates in achieving continence are reported to be as high as 80%. Patients who experience only partial improvement can be supplemented by endoscopic bulking injections. All patients who undergo bladder neck reconstruction with or without a sling will need to catheterize either through the urethra or using a continent abdominal stoma.
4. Artificial urinary sphincter: Placement of an inflatable cuff around the bladder neck offers up to 90% improvement in continence in both girls and boys (Fig. 11-3). Although highly successful, complications include device failure (in about 12%) because of erosion of the cuff. Placement of the artificial sphincter should be done only in patients with normal bladder capacity and compliance because of the risk of the bladder becoming noncompliant after occluding the outlet (seen in as many as 30% of pateints).

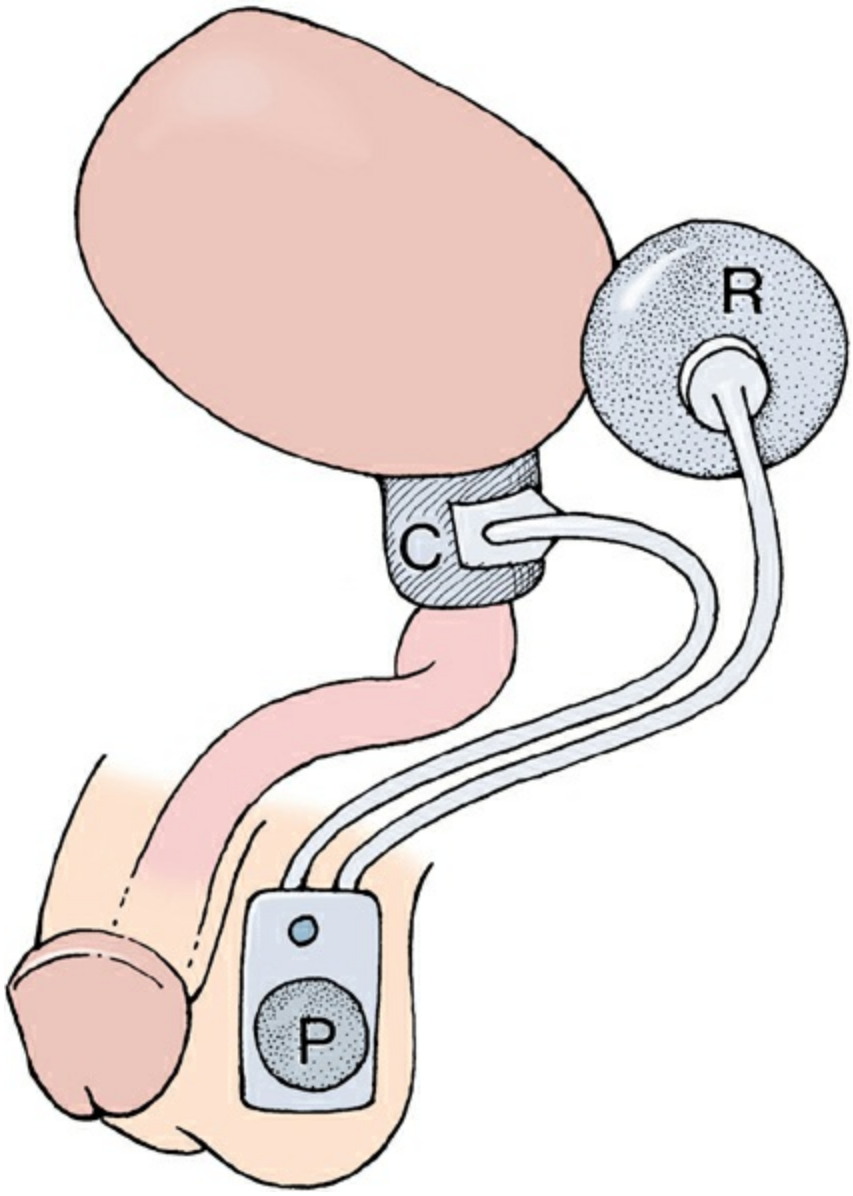

Fig. 11-3 Diagram of an artificial urinary sphincter consisting of three parts. The cuff (C) is placed around the bladder neck or prostatic urethra (in males) and is connected to a pump (P) in either the scrotum or labium, and a fluid reservoir (R) implanted beneath the rectus muscle. Fluid is pumped from the cuff into the reservoir which then passively re-fills the cuff over 60 to 90 seconds. In children who perform CIC, the cuff is pumped open and catheterization is easily done.

C. Vesicoureteral Reflux

Between 40% and 65% of patients with spina bifida will have vesicoureteral reflux (VUR). This is usually due to increased intravesical pressures resulting from detrusor sphincter dyssynergia or a poorly compliant bladder.

Treatment is directed toward improving urine storage (decreasing bladder pressure) and elimination by giving anticholinergic medication and CIC. Persistent reflux must then be managed on an individual basis. Low-dose antibiotic prophylaxis is usually given to all children with reflux. Surveillance alone can be offered to children with low-grade reflux who do not have symptomatic urinary infections or renal scarring, and are compliant with bladder management. Should surgical intervention become necessary because of breakthrough infections or worsening hydronephrosis, an endoscopic antireflux procedure (ureteric injection of Deflux) may be a reasonable first choice if the bladder is compliant. However, the gold standard remains surgical ureteral reimplantation. If surgical intervention is undertaken to improve capacity or continence, it is prudent to consider reimplantation at that time.

D. **Bacteriuria**

Bacteriuria is found in many children with spinal dysraphism, especially those who perform CIC, and is termed "asymptomatic bacteriuria." These patients *do not* require antibiotic therapy or prophylactic suppression unless there is documented vesicoureteral reflux or symptoms such as fever, dysuria, or new-onset incontinence. In the absence of vesicoureteral reflux, there is little risk of renal scarring.

E. **Renal Function**

Elevated detrusor pressures and recurrent urinary tract infections are the primary risk factors for renal deterioration and may be prevented by appropriate care of the lower tract. Because serum creatinine and renal sonography may not provide a consistent measure of early renal injury, a more accurate measure may be obtained with a nuclear renal scan (DMSA [Technetium-dimercaptosuccinic acid] or MAG-3 [Technetium-mercaptoacetyltriglycine]). It is advisable then to obtain a nuclear renal scan as a baseline in children who have not

been evaluated in the neonatal period and who are at risk for renal damage from recurrent infection. We recommend renal sonography and urinalysis every 3 months for the first year of life, every 12 months thereafter, and with any change in urinary status (incontinence, infection, or problems with catheterization).

F. **Bowel Management**

The management of fecal elimination can be a significant challenge to patients and caregivers. All patients require a bowel program which includes dietary modification, cathartics and/or enemas, and possible digital stimulation and manipulation. For patients in whom conservative management fails, creation of a continent abdominal conduit to the cecum may enable antegrade delivery of a large-volume enema to clear the colonic contents (Malone antegrade continence enema or “MACE” procedure, Fig. 11-4). The appendix is ideal for use as the conduit, but if absent, other bowel segments can be used, or a percutaneous cecostomy tube (“button”) can be placed by interventional radiographic means. In our experience we have found that children in whom we have aggressively treated constipation early on (birth to 3 years) have greater success with training for stool continence. Therefore, all constipation should be treated aggressively in this population despite age or desire for continence.

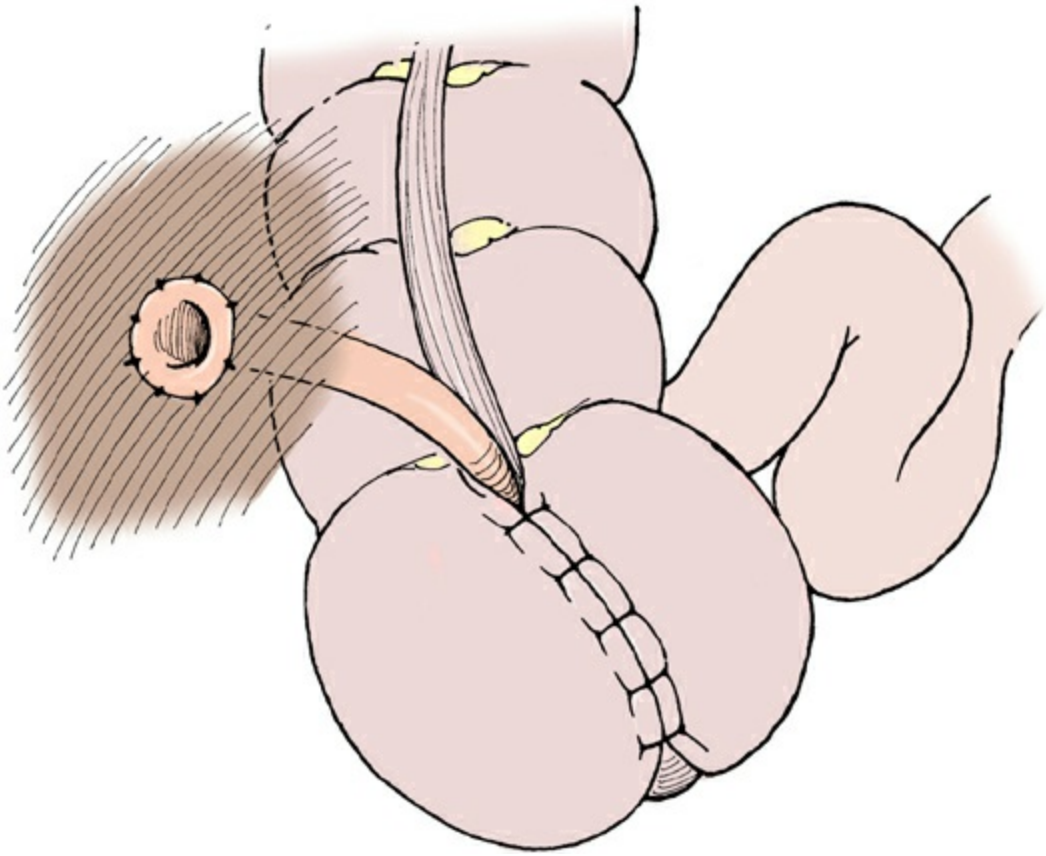

Fig. 11-4 The Malone antegrade continence enema (MACE) procedure utilizes the appendix as a continent catheterizable channel to deliver a bolus of fluid (such as tap water) to help "flush" out the colonic contents in patients with severe refractory neuropathic constipation.

G. Sexual Function and Fertility

The majority of spina bifida adults report being sexually active. Adolescents, however, have more than the usual problems of developing a sexually desirable identity when concerns about bowel or bladder continence persist into the teenage years. For this reason, we encourage measures to improve continence before the onset of puberty, which commonly comes about early in female spina bifida patients. Caregivers should pay careful attention to this often-overlooked area. These patients frequently have no role model and need open dialogue to support their growth and independence.

Fertility in males with spina bifida is less likely than in the general population due to inadequate erectile function,

semen quality, and factors of socialization. However, each male patient must be approached individually with a goal toward maximizing his available function and counseled regarding the possibility of paternity. Modern treatment of erectile dysfunction and infertility may improve the possibilities for these patients greatly. All these patients should be given appropriate counseling regarding sexually transmitted diseases and pregnancy. Both males and females need to be given information on how to obtain non-latex condoms.

H. **Latex Precautions**

In the era of latex-free hospital environments, less latex exposure to children with neurogenic bladder means that life-threatening anaphylactic reactions attributable to latex allergy are extremely rare. Products containing latex such as gloves, urethral catheters, tourniquets, IV injection ports, anesthesia ventilation bags, blood pressure cuffs, and adhesive tape should always be avoided in this group.

VI. OCCULT SPINAL DYSRAPHISM

See Table 11-1.

A. **Signs**

Sometimes defects of the spinal cord may not be apparent on physical examination and become manifest only after the onset of urologic, neurologic, or orthopedic problems. Occasionally the only clue is a prominent sacral dimple or sinus tract, a tuft of hair or prominent pigmentation, or presence of a lipoma. Any one of these signs should prompt further evaluation. The presenting signs and symptoms are often insidious. New onset of urinary incontinence, changes in voiding pattern, or urinary tract infection in an individual who has been voiding normally or who has a known diagnosis of spina bifida suggests a possible problem. This is usually a tethered spinal cord characterized by a short, thickened filum terminale, which prevents the ascent of the conus medullaris during

development.

B. **Workup**

1. Spinal ultrasound: In the neonate or infant, spinal ultrasound examination can reliably reveal low position and a nontapered, bulbous appearance of the conus, dorsal location of the cord within the bony canal, solid or cystic masses in the distal canal or soft tissue of the back extending toward the canal, patulous distal thecal sac, and a thick filum terminale. This study is only possible in infants.
2. Magnetic resonance imaging: MRI characterizes spinal cord involvement more accurately. It is the diagnostic procedure of choice in older children in whom bone maturation precludes accurate sonography.

C. **Intervention**

Whether or not early neurosurgical intervention ameliorates voiding dysfunction by relieving spinal cord compression or tethering remains controversial. If detected in infancy, urologic deterioration can be prevented in most and improved in many of those who present with dysfunction. With release of spinal cord tethering, one can expect a 50% improvement in voiding symptoms and more than 50% resolution of detrusor hyperreflexia. Older patients who present with neurologic changes are less likely to improve. Overall, patients with neuropathic bladders from occult lesions should be managed in the same fashion as those with overt spinal dysraphism.

VII. PRENATAL INVENTION FOR MYELOMENINGOCELE

As noted, urologic complications are a main source of morbidity in patients with spinal dysraphism. Fetal animal studies demonstrated that prolonged exposure of the open spinal cord resulted in defective nerve development, and that

fetal closure reduced morbidity. This led to the recent Management of Myelomeningocele Study (or MOMS trial), a randomized prospective trial with in-utero repair performed through a small hysterotomy. The study showed that fetal intervention is beneficial for decreasing the need for ventriculoperitoneal shunting, a lower incidence of Chiari malformation, and improved musculoskeletal outcomes. Unfortunately, the effect of fetal back closure on voiding function does not enjoy the same success.

Finally, some have argued that vaginal delivery itself may cause trauma to the spinal cord; however this has not been studied in a prospective randomized trial. Regardless, most centers recommend caesarean deliveries in most cases.

VIII. CONCLUSION

Urologic care of patients with spinal dysraphism focuses on preserving renal function, establishing urinary and bowel continence, promoting the development of normal sexuality, and a commitment to the minimum of surgical intervention. Early intervention (both diagnostically and therapeutically) and patient education help guarantee the most successful outcome. Intermittent catheterization with close clinical follow-up should be instituted early to prevent, rather than treat, the complications of neurogenic bladder dysfunction.

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Adzick NC, Thom EA, Spong CY, et al. A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med* 2011;364(11):993–1004.

MacLellan DL, Bauer SB. Neuropathic dysfunction of the lower urinary tract. In: *Campbell-Walsh urology: Pediatric urology*, 10th ed. Elsevier-Saunders: New York; 2015.

12 Prenatal Urologic Diagnosis and Maternal Counseling

Barry A. Kogan

I. INTRODUCTION

With the advent of the widespread use of prenatal ultrasound in clinical practice, urologic conditions are being diagnosed in many infants before birth. Because ultrasound is performed so commonly, the impact of these diagnoses has been considerable. It remains unclear however, whether this early diagnosis results in benefit to the neonate or merely increased anxiety over testing. In the majority of cases, the parents can be reassured that postnatal evaluation is all that is needed and that their infant will have a good prognosis.

II. INCIDENCE

Urologic anomalies are found in about 0.4% of pregnancies. Of these, hydronephrosis is found in about half (see Chapter 13).

III. FINDINGS

Urologic findings may range from mild hydronephrosis, which is essentially a normal finding, to significant hydronephrosis resulting from any type of obstructive uropathy (see Chapter 13, Figs. 13-1, 13-2, and 13-3). In rare cases, renal tumors or congenital anomalies such as exstrophy and epispadias can be found.

IV. GENERAL TREATMENT

After initial diagnosis, a more extensive ultrasound survey is performed to confirm the diagnosis, look for associated findings, and, in the case of renal anomalies, to monitor the amount of amniotic fluid. In rare cases, some intervention is warranted in utero, for example, aspiration of an enormous cystic mass or in very rare cases, placement of a vesicoamniotic shunt. It is very rarely indicated to deliver the baby early. In the overwhelming majority of cases, no intervention is needed before birth. In most, a postnatal evaluation is recommended. However, the overall benefits of prenatal diagnosis for genitourinary lesions are unproven.

V. SPECIFIC DIAGNOSES

A. **Hydronephrosis**

Easy diagnosis in utero. The following parameters are important.

1. The amount of amniotic fluid (correlates loosely with renal function).
2. Unilateral or bilateral (unilateral is less concerning due to normal contralateral kidney).
3. Evaluate the amount of hydronephrosis (generally by measuring the anterior posterior [AP] diameter of the renal pelvis). An AP diameter greater than 10 mm of the renal pelvis in the third trimester warrants a postnatal evaluation (see below).
4. Amount of renal parenchyma.
5. Corticomedullary differentiation (when present this suggests good renal function).
6. Echogenicity (when present this suggests renal dysplasia).
7. Cortical cysts (when present this suggests renal dysplasia).
8. Ureteral dilation (suggests diagnosis at the bladder or urethral level) and requires a postnatal evaluation.

9. Bladder distention (suggests diagnosis at urethral level).
10. Gender (boys may have posterior urethral valves).

Postnatally, patients with significant prenatal hydronephrosis as defined by an AP diameter greater than 10 mm in the third trimester or ureteral dilation should have a sonogram and a consideration given to a VCUG (33% incidence of reflux, especially if there is ureteral dilation) at several weeks of age.

In some centers, prophylactic antibiotics (amoxicillin or cephalexin [Keflex]) are recommended until it is proven that there is no reflux. This is particularly true if there is ureteral dilation.

As a corollary, a prenatal diagnosis of hydronephrosis with an AP diameter less than 10 mm in the third trimester rarely if ever results in a clinically significant postnatal outcome such as loss of renal function, pain, or progressive hydronephrosis. These patients have a slightly dilated yet normal functioning kidney. They do not need postnatal evaluation unless clinical suspicion such as a urinary tract infection, hematuria, or pain results.

Circumcision is suitable for boys with significant prenatal hydronephrosis, and in some cases, may be recommended as it reduces the rate of UTIs.

Generally patients with a prenatal hydronephrosis have an excellent prognosis.

B. **Urethral Valves**

This is diagnosed by hydronephrosis, bladder distention, and the “keyhole” sign on ultrasound. The same findings as above are important, but especially amniotic fluid and renal parenchymal changes. If amniotic fluid is normal and there is no sign of renal dysplasia on renal ultrasound, then the most appropriate treatment is to defer treatment until after birth. At that time, the neonate should have catheter drainage, VCUG, and resection of valves if he is large enough (alternatively a temporary vesicostomy can

be used to bypass the blockage). In rare cases, consider fetal intervention (see below). The prognosis depends on the degree of renal dysplasia and is generally determined after birth if amniotic fluid is normal.

C. **Multicystic Dysplastic Kidney**

This is easily diagnosed in utero. The main findings are chaotic configuration of the kidney, multiple cysts that do not communicate, and minimal, if any, normal renal parenchyma. This is generally associated with a normal contralateral kidney and normal amniotic fluid. Postnatally, we recommend ultrasound to confirm the diagnosis. If there is any doubt in the diagnosis, a nuclear scan will confirm that the kidney is nonfunctional. Although we used to perform VCUG in all (25% of children have contralateral reflux into the solitary kidney), we no longer recommend this as these children rarely have clinical issues. There are rare cases of hypertension requiring nephrectomy but in most cases, once the diagnosis is confirmed, these children do not need urologic follow-up (the primary care doctor can check for hypertension). The multicystic kidney will involute and there are no clinical sequelae. Counseling is similar to any patient with a solitary kidney.

D. **Duplications, Ectopic Ureters, or Ureteroceles**

These are often diagnosed in utero by hydronephrosis of one pole of a kidney (typically the upper pole), ureteral dilation, and/or a classic ureterocele configuration in the bladder. Provided amniotic fluid is normal, no further in utero treatment is needed. Prophylactic antibiotics and postnatal ultrasound and VCUG are appropriate (see Chapter 14 for treatment).

VI. PRENATAL TREATMENT AND MATERNAL COUNSELING

A. **Urinary Tract Obstruction**

Prenatal intervention is appropriate in only the exceptional urologic case. The most common

circumstance is in cases of severe bilateral hydronephrosis with reduced amniotic fluid in the early second trimester. In those instances, a careful fetal survey (to rule out other anomalies) and amniocentesis (for chromosome analysis) are essential before consideration of intervention. An analysis of the degree of renal injury is the next step and this is done first by ultrasound. In general, acceptable renal function is associated with normal amniotic fluid; however, when the fluid is reduced other assessments are needed. The amount of renal parenchyma can be assessed easily. More specifically though, the lack of corticomedullary differentiation and the presence of increased echogenicity and cortical cysts are all associated with renal dysplasia. If the kidneys are acceptable by ultrasound, fetal urine samples are obtained (some feel it is best to drain the bladder 3 days in a row to obtain fresh urine). Although many tests have been proposed, low sodium and low osmolarity (indicative of enough tubular function to reabsorb urine) are associated with salvageable renal function. In these highly selected patients, after counseling of maternal as well as fetal risks, consideration may be given to in utero intervention. Although there are reports of fetal cystoscopic treatment, the most common intervention is a fetal vesicoamniotic cavity shunt (usually via percutaneous catheter placement). This is done under local anesthesia with maternal sedation and with careful monitoring and medications to reduce the risk of premature delivery. Despite this, many of these infants do deliver early. Long-term results are mixed. There is a benefit in preventing pulmonary hypoplasia (and thereby increasing neonatal survival), but it is still unclear whether renal functional improvement is achieved. This brings up the ethical concern that these children may be surviving due to therapy, but doomed to neonatal renal failure with all its attendant problems.

B. **Myelodysplasia**

Prenatal diagnosis of this condition is increasing owing to increased use of maternal screening for α-fetoprotein. Based on this, prenatal open surgical hysterotomy and fetal myelomeningocele repair has been done in several centers as part of a multi-institutional National Institutes of Health (NIH)–sponsored study. Results suggest that the rate of ventriculoperitoneal shunting is reduced in these patients, but neurogenic bladder dysfunction is still a problem. Much longer-term follow-up is needed.

VII. SUMMARY

Fetal diagnosis of urologic anomalies is common. Although the benefits are not proven fully, the prevalence of prenatal ultrasound means that many children will be diagnosed. In most instances, parental education should emphasize the excellent prognosis and the need for nonemergent postnatal evaluation. In extremely rare cases, fetal intervention may be warranted.

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Adzick NS, Thom EA, Spong CY, *et al*. A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med* 2011;364:993–1004.

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13 Neonatal Hydronephrosis

Barry A. Kogan

I. DIAGNOSIS

The diagnosis of neonatal hydronephrosis is most often made based on an incidental finding detected on prenatal ultrasound done for another reason. Occasionally, an infant may be brought to the physician with a flank mass, urinary tract infection, or rarely with hematuria. Older children most often present with intermittent pain and vomiting.

A. **Incidence**

The incidence of hydronephrosis varies depending on the cut-off level for renal anteropelvic diameter that is used during prenatal sonographic evaluation. Because of high false-positive rates, pelvic diameters below 10 mm in the third trimester are generally not considered significant.

Although the incidence of some renal enlargement on prenatal ultrasound is 1% to 1.4%, most of these cases resolve after birth and the incidence of significant urinary tract disease is 0.2% to 0.4%.

B. **Differential Diagnosis of Prenatal Urinary Tract Dilation**

See Figure 13-1.

1. Ureteropelvic junction (UPJ) obstruction (approximately two-thirds of cases) (Fig. 13-2A).
2. Vesicoureteral reflux (approximately one-fourth of cases).
3. Ureterovesical junction obstruction (will have a dilated ureter) (Fig. 13-2B).

Multicystic dysplastic kidneys (multiple renal cysts
4. that do not connect to each other).
5. Posterior urethral valves (will have a markedly abnormal bladder also).
6. Other diseases like prune belly syndrome or polycystic kidney disease (rare).

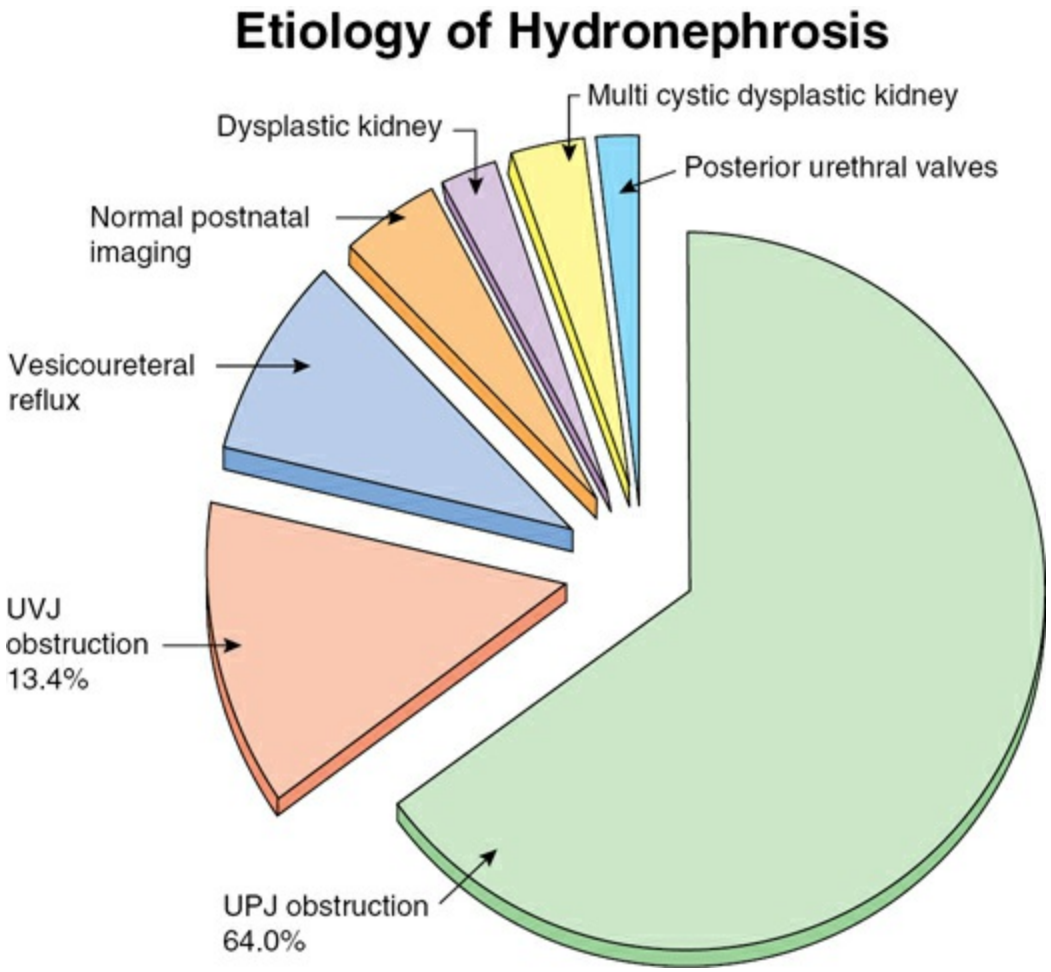


Fig. 13-1 Etiology of neonatal hydronephrosis. UPJ, ureteropelvic junction; UVJ, ureterovesical junction.

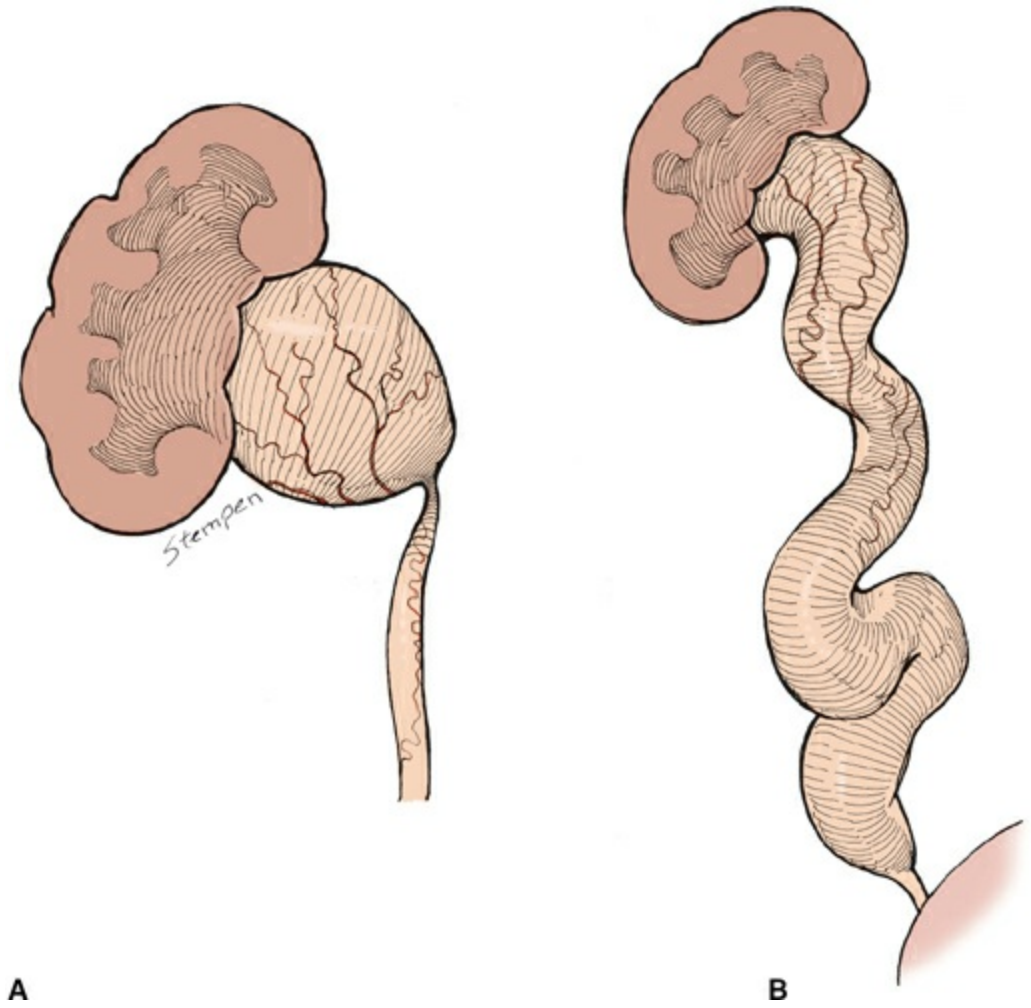


Fig. 13-2 A: Ureteropelvic junction obstruction. B: Ureterovesical junction obstruction/megaureter.

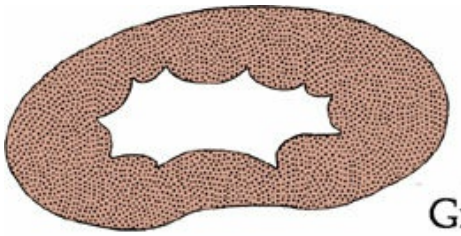
C. **Etiology of UPJ Obstruction**

The exact cause is debatable, but a scarred or adynamic segment of the proximal ureter often leads to a kink at the UPJ that may be responsible for the obstruction. Less common causes are congenital mucosal folds or polyps of the upper ureter. In older children, especially girls, an extrinsic obstruction from a crossing artery to the lower pole of the kidney is more common.

II. EVALUATION OF NEONATAL HYDRONEPHROSIS

A. **Ultrasound**

1. Unless there is severe bilateral hydronephrosis, dilated ureter, or dilated posterior urethra on prenatal sonograms, postnatal ultrasound should be postponed until the physiologic dehydration of newborn has resolved (usually after 72 hours).
2. The grading system of the Society of Fetal Urology has been used and is common in the literature (Fig. 13-3 and Table 13-1). It has been recently updated but it is unclear how accepted the update is. A relatively universal method to define hydronephrosis is to simply measure the greatest dimension of the renal pelvis. As mentioned above, renal pelvic diameters greater than 10 mm in the third trimester should be considered clinically relevant and require further evaluation. Caution is required as, quantification of the hydronephrosis is dependent on the ultrasound operator, and hydration status and positioning of the patient. The status of the urinary bladder can also affect the degree of hydronephrosis (when possible, hydronephrosis should be assessed when the bladder is both full and empty).



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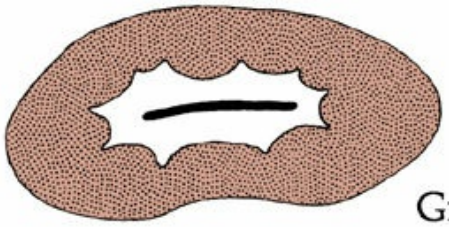

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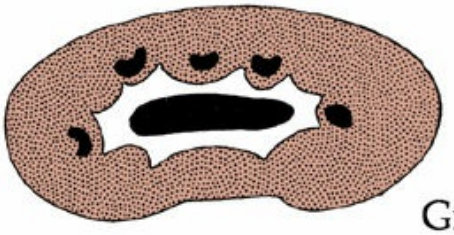

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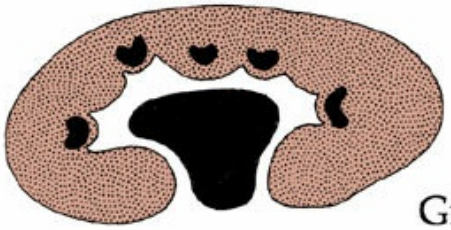

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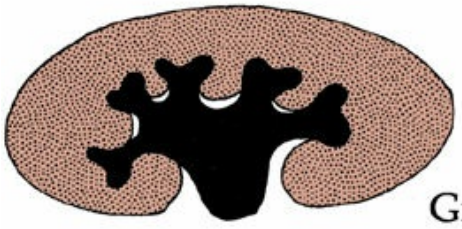

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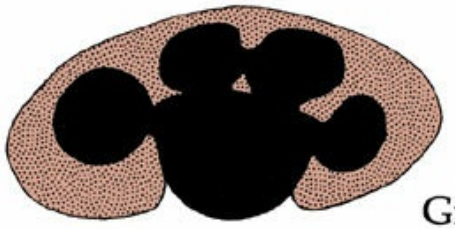


Grade IV

Fig. 13-3 Society of Fetal Urology grading system.

TABLE 13-1 Ultrasound Grading System for Hydronephrosis

Grade of Hydronephrosis	Central Renal Complex	Renal Parenchymal Thickness
0	Intact	Normal
1	Slight splitting	Normal
2	Evident splitting Complex confined within renal border	Normal
3	Wide-splitting pelvis Dilated outside renal border and calices	Normal
4	Uniformly dilated Further dilation of renal pelvis and calices	Thin

B. **Voiding Cystourethrography (VCUG)**

Previously most clinicians recommended a VCUG in every infant with neonatal hydronephrosis because the sonography is not a good predictor of vesicoureteral reflux and 25% to 33% of these children will have reflux. Some have counterargued that this reflux is not clinically significant and a VCUG is not needed. We currently do not recommend a VCUG unless a dilated ureter or distended bladder are seen or in cases of severe hydronephrosis.

C. **Radionuclide Scanning**

Not all urinary tract dilation is a sign of significant obstruction. Although the size of the renal pelvis is of some value, it is not definitive. To help distinguish “obstructed” kidneys from those that are merely dilated, the most common test is the diuretic renogram. This test

estimates the relative renal function of the two kidneys and gives an estimate of the "washout" of radioisotope from the kidney. This washout correlates in a limited way with the degree of obstruction (although the size of the renal pelvis and the amount of diuresis are both important in determining the rapidity of the washout). The test requires hydration and the injection of a radioisotope that is excreted in the urine, as well as a catheter draining the bladder in young children. The two principle choices are given below.

1. 99m-technetium-diethylenetriaminepenta acetic acid (DTPA): DTPA is cleared by glomerular filtration and is not reabsorbed or excreted by tubules. Hence it provides a good measurement of glomerular filtration rate.
2. 99m-technetium-mercaptoacetyltriglycine (MAG-3): MAG-3 is the first choice in children with poorly functioning kidneys since it is mostly cleared by tubular excretion. It is also a good indicator of effective renal plasma flow.

It is important to recognize the technique and related pitfalls. After the administration of radiopharmaceutical agent (DTPA or MAG-3) and taking serial images with a gamma camera, the regions of interest (ROI) over both kidneys and the background are defined. The amount of radioisotope excreted in the urine (the number of counts in each ROI) over time is calculated and then the background activity is subtracted from the kidney counts. Furosemide is administrated when the pelvis is full (usually 20 to 30 minutes after the radioisotope is injected to develop time-activity washout curves (see Chapter 14, Fig. 14-2). The rapidity of washout is correlated with the degree of obstruction. Some authors have tried to use the half-time clearance of radioisotope from the collecting system ($t_{1/2}$) as an indicator of obstruction ($t_{1/2}$ more than 20 minutes, obstructed; $t_{1/2}$ of 10 to 20 minutes, indeterminate; $t_{1/2}$ less than 10 minutes, nonobstructed),

but it is not as objective as the clinician would like since it is affected by the following.

a. The degree of obstruction (severe obstruction may cause delays in peak renal activity with reduction in renal filtration pressure).
b. The compliance of renal pelvis (a highly dilated or compliant pelvis may not respond well to diuretic).
c. The dosage, timing, and response to furosemide (poorly functioning kidneys may not respond).
d. The degree of hydration (dehydration may delay excretion).
e. Drainage of the bladder (a full bladder may delay renal washout).
f. The position of the patient (some kidneys drain better in the prone position).

In sum, the data collected in radionuclide scanning must be interpreted depending not only on computer analysis, but also on clinical status of the patient. The age of 4 to 6 weeks is usually appropriate for the test time, but in case of earlier need of evaluation, MAG-3 should be the choice of radioisotope.

Although not useful to determine the degree of obstruction, 99m-technetium-dimercaptosuccinic acid (DMSA) is the most reliable technique to show the relative renal function (it remains bound to proximal tubular cells).

III. MANAGEMENT OF UPJ OBSTRUCTION IN INFANTS

A. Natural History of UPJ Obstruction (Conservative Management)

Unfortunately, there is no currently available method to predict which kidney will deteriorate or remain unaffected in children with hydronephrosis. In fact, many of these infants do very well over a long period of time when followed up conservatively. The ultimate goal of treatment is to preserve the renal function before

contralateral compensatory hypertrophy occurs and to determine which kidney will truly benefit from surgery. The facts are as follows.

1. The conversion rate to the surgery in an observation group of high-risk kidneys is approximately 25%. Kidneys with renal pelvic diameter greater than 50 mm have a high likelihood of renal deterioration; hence early repair seems to be the best choice for this group.
2. Kidneys with renal pelvic diameter smaller than 20 mm, even with an obstructive pattern on renography may be followed up with serial ultrasounds and diuretic renography.
3. When the hydronephrotic kidney has a relative renal function less than 40% or has a loss of function greater than 10% on serial scans, surgery is recommended.
4. Urinary tract infections should be documented carefully since there are no specific symptoms in this age group. Breakthrough infections may cause rapid renal deterioration; hence surgery is also recommended in such cases. The use of prophylactic antibiotics is controversial in cases with isolated hydronephrosis and without ureteral dilatation or VUR.
5. Formation of renal calculus is also an indication for surgery.

The diagnosis of bilateral UPJ obstruction should be made with caution and only after ruling out the possibilities of posterior urethral valves and VUR, in which the ureters are also dilated and the bladder is usually affected. Relative renal function is not helpful in bilateral obstruction since both kidneys are affected to some degree.

B. **Surgery**

Anderson-Hynes dismembered pyeloplasty is the gold

standard of techniques used for the repair of UPJ with an overall success rate of more than 95%.

Endopyelotomy (either balloon cautery or cold knife) is not routinely used in the pediatric population. Also it is not helpful when an extrinsic factor (aberrant vessel) or renal calculus is present.

Laparoscopic (usually robot-assisted) pyeloplasty is becoming a common alternative to open surgery in the pediatric population. Typically the hospital stay and recovery time are similar, but the cosmetic appearance of multiple small incisions compared to a flank scar is generally considered better.

MULTICYSTIC DYSPLASTIC KIDNEYS (MCDK)

This is a severe form of renal dysplasia in which the kidney has virtually no function. On ultrasound, there is a very thin and abnormal renal parenchyma, surrounded by multiple cysts of various sizes that do not connect, nor do they connect to the renal pelvis.

I. DIAGNOSIS

Most cases of MCDK are diagnosed incidentally during prenatal sonography. In more unusual cases, it may be diagnosed after discovery of a palpable or visible abdominal mass in the infants. MCDK must be distinguished from the hydronephrosis caused by UPJ obstruction, as the latter may be repairable. The diagnosis may be made by ultrasound with good reliability. The existence of infundibular connections between calyces and the renal pelvis is good evidence of hydronephrosis and not MCDK (Fig. 13-4).

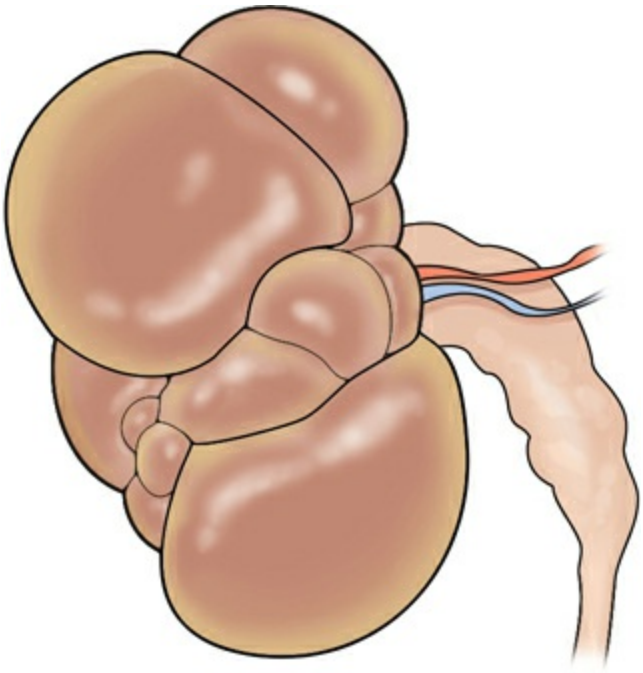


Fig. 13-4 Schematic of gross multicystic dysplastic kidney and ultrasound images.

II. EVALUATION

A. **Renal Scan**

There is an increased incidence of UPJ obstruction (3% to 12%) in the contralateral (solitary functional) kidney. A radionuclide scan is recommended if there is any question of UPJ obstruction in the affected kidney. In hydronephrosis, a rim of functioning parenchyma is seen. In MCDK, there is little or no uptake of radionuclide.

B. **VCUG**

Because there is a high rate of reflux in the contralateral (solitary functioning) kidney (18% to 43%), in the past, a VCUG was recommended. Because the contralateral reflux rarely has any clinical sequela, it is rarely performed unless there is a dilated ureter.

III. NATURAL HISTORY

When multicystic kidneys occur bilaterally, it is not compatible with life and these children die immediately after birth from pulmonary hypoplasia. Most cases are unilateral

and virtually all become smaller over time. When the involution occurs, the cyst fluid disappears and the dysplastic cells may remain in place. However, in most cases the involution is so severe that there may not be any identifiable tissue on the ultrasound. It is highly likely that this happens in most cases over time, as the condition is extremely rare in adults.

Hypertension occurs in rare cases, so the infant's blood pressure should be checked periodically. When hypertension has been reported, nephrectomy has been curative.

The presence of dysplastic cells has led to the theory that these children have an increased risk of malignancy. In fact, the development of Wilms' tumor in these patients is very rare. Moreover, annual ultrasound is probably insufficient for early detection of the rare tumor. Although some recommend nephrectomy to prevent this, most clinicians avoid any intervention for this benign condition.

IV. MANAGEMENT

When detected prenatally, unilateral multicystic kidney can be followed relatively unaggressively. Unless it is massive in size affecting pulmonary function, there is no need for any change in the routine treatment prenatally or in the mode of delivery.

Postnatally, an ultrasound should be obtained to confirm the diagnosis. Once the diagnosis is confirmed, no intervention is needed. Indeed, other than routine blood pressure checks, no follow-up is needed. Some would suggest that some observation is appropriate until the kidney involutes and/or there is contralateral compensatory hypertrophy. In an era in which cost-effective medicine is essential, routine annual ultrasound is both costly and of minimal benefit.

Families should be counseled regarding the risks of a solitary kidney. Current American Academy of Pediatrics

(AAP) recommendations are that they should avoid contact sports for concern of injuring the solitary kidney. On the other hand, sports injuries sufficient to result in nephrectomy are increasingly rare (see Chapter 28).

RECOMMENDED READING

Cardona-Grau D, Kogan BA. Update on multicystic dysplastic kidney. *Curr Urol Rep* 2015;16:67.

Nguyen HT, Benson CB, Bromley B, *et al*. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD) classification system. *J Pediatr Urol* 2014;10:982–998.

14 Hydroureteronephrosis: Ureteroceles, Duplications, Ureteral Ectopy

Laurence S. Baskin

I. DEFINITIONS

A. **Hydronephrosis:** an anatomic entity describing an enlargement or dilation of any portion of the collecting system of the kidney.
B. **Pelviectasis:** dilation of the renal pelvis only.
C. **Caliectasis:** dilation of the renal calyces only.
D. **Pelvocaliectasis:** dilation of both the pelvis and calyces.
E. **Pyelocaliectasis:** equivalent to caliectasis.
F. **Hydroureteronephrosis:** includes dilation of any portion of the collecting system of the kidney, plus dilation of the ureter as well.
G. **Ureterectasis or ureteronephrosis:** dilation of the ureter only.
H. **Obstruction:** a restriction of urinary outflow. A complete obstruction will lead to renal damage. An incomplete obstruction may be *physiologic* (i.e., normal and not affecting renal function) or *pathologic* (i.e., abnormal and leading to renal injury). Obstruction and hydronephrosis are not synonymous. *A patient may have an enlarged renal collecting system but not have a pathologic obstruction*.

II. INCIDENCE

Hydronephrosis is present in up to 1.4% of fetuses and persists postnatally in half (0.7%).

III. SIGNIFICANCE

One must distinguish whether the hydronephrosis or ureteronephrosis is secondary to an ongoing obstruction (in which case there may be progressive renal deterioration), or secondary to a prior obstructive event that both occurred and resolved antenatally (in which case there will be no further renal damage). In the former, if the obstruction is severe, surgical treatment to correct the obstruction may be necessary to preserve renal function; in the latter, surgical treatment is unnecessary.

IV. ETIOLOGY

Before one can debate whether the child with hydronephrosis needs surgical treatment, one must first determine the etiology of the hydronephrosis. Sometimes the etiology is straightforward (e.g., posterior urethral valves, ureteroceles) and thus the treatment options are clear (i.e., relieve the obstruction). In most cases, however, the hydronephrosis is secondary to a ureteropelvic (64%) or ureterovesical (13%) junction obstruction. In such cases, the treatment options are less clear. Many of these patients are not truly pathologically obstructed and the hydronephrosis or ureteronephrosis may be transient, resolving in time or persisting without clinical consequence; thus surgical intervention is not warranted or necessary.

Vesicoureteral reflux and posterior urethral valves are discussed in Chapters 7 and 15. Neonatal hydronephrosis is discussed in Chapter 13.

A. Ureteropelvic Junction (UPJ) Obstruction

1. Incidence: The UPJ is the most common site of obstruction in the upper urinary tract (Fig. 14-1). Approximately 64% of the 0.7% of children born with hydronephrosis will have a UPJ obstruction.

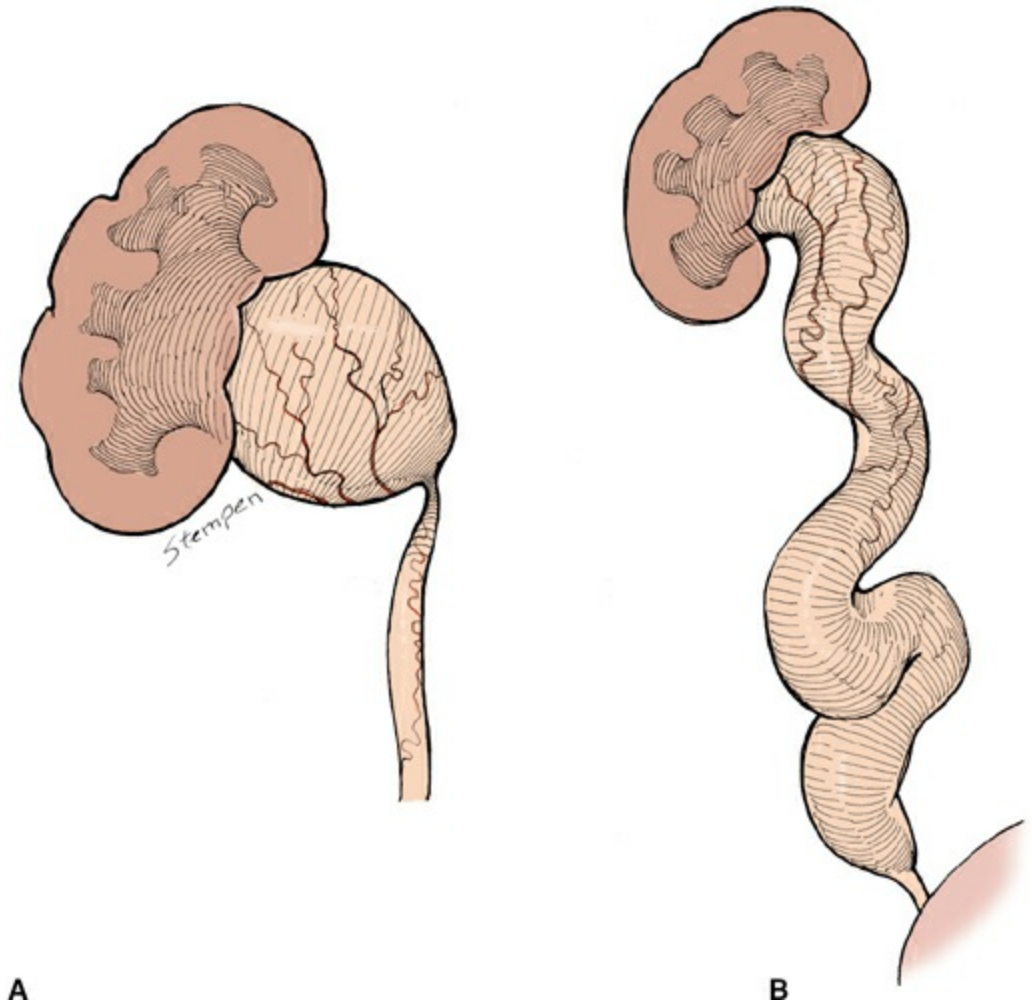


Fig. 14-1 Ureteropelvic junction obstruction (A) as compared to congenital megaureter (B).

2. Pathophysiology: Successful conduction of urine from the renal pelvis to the ureter requires an anatomically patent ureteropelvic junction as well as an undisturbed transmission of peristaltic contractions in the proximal ureter. Thus, UPJ obstruction can result from an anatomic abnormality or from poor conduction of peristalsis (Fig. 14-1A). The abnormality can be either *extrinsic* or *intrinsic*. Intrinsic obstruction secondary to a narrow segment with muscular discontinuity is the most common cause. Extrinsic causes include aberrant vessels, kinks, or a high insertion of the ureter into the pelvis. There may also be a combination of intrinsic and

extrinsic obstruction, for example, an intrinsic ureteral obstruction leading to a dilated pelvis which then results in a kink in the ureter (extrinsic). Rarely, a ureteral polyp may grow from just below the ureteral pelvic junction and intermittently obstruct the flow of urine by a ball valve mechanism.

3. Clinical presentation
    a. Infants: Most cases of UPJ obstruction are diagnosed in utero (Chapter 13). If *not* noted in utero, infants will present with abdominal mass, hematuria, urinary tract infection, or gastrointestinal discomfort. Of all abdominal masses in infants less than 1 year of age, 50% are renal in origin and 40% of these are secondary to a UPJ obstruction.
    b. Older children: Older children will present with abdominal or flank pain, chronic nausea, or hematuria. This may occur after excessive hydration or following mild trauma, or urinary tract infection. Younger children tend to have more generalized lower abdominal pain, and older children will have more conventional flank pain (Dietl's crisis). The flank pain may worsen with diuresis (e.g., after caffeinated beverages). Any child with gross hematuria after minor trauma should be evaluated for a UPJ, as should any boy with a frank urinary tract infection.
4. Associated anomalies: Patients with imperforate anus, contralateral multicystic kidney disease, congenital heart disease, VACTERL (vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities) syndrome, or esophageal atresia should be screened with a renal ultrasound to rule out hydronephrosis. Also, 10% of patients with UPJ obstruction have ipsilateral ureterovesical reflux.
5. Workup

a. Hydronephrosis discovered antenatally: see Chapter 13.
b. In older children:
    (1) Ultrasound: Although an ultrasound should be performed as a screening test for an older child with a suspected UPJ obstruction, it may not always show hydronephrosis. If it does not show hydronephrosis, it should be repeated when the patient is having pain. If the ultrasound is done during an episode of pain, it will almost always show hydronephrosis if a UPJ obstruction is present.
    (2) Diuretic renography: A MAG 3 Lasix renogram is performed if the ultrasound shows significant hydronephrosis (society of fetal urology grade 3 or 4). This will document the function of the normal and affected kidney and may on occasion provoke pain (secondary to the diuresis from the Lasix) if the obstruction is intermittent (Fig. 14.2).

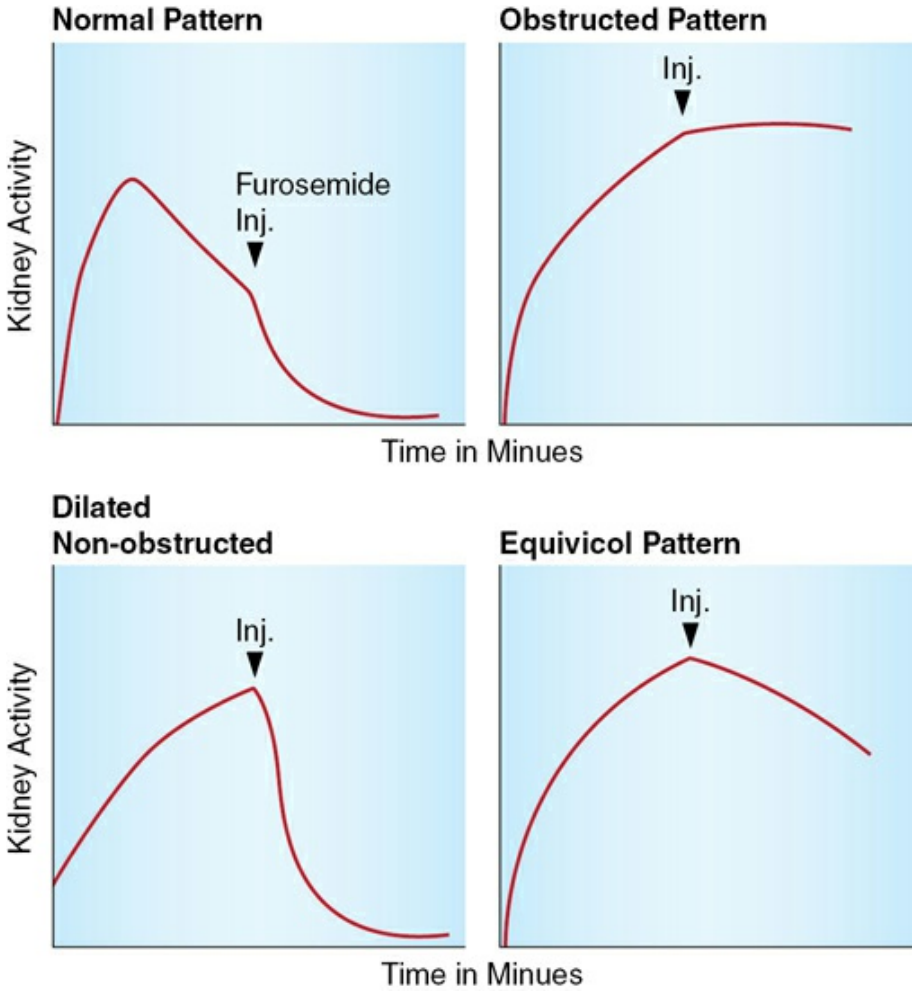


Fig. 14-2 Obstructed versus nonobstructed washout curves on diuretic renography.

(3) Voiding cystourethrogram (VCUG): Historically, all patients with suspected UPJ obstruction underwent a VCUG. Without evidence of a dilated ureter on sonography, the yield in detecting clinically significant reflux in either the affected kidney or contralateral kidney is minimal. Therefore in potty-trained children, routine VCUG is no longer indicated.

(4) CT scan: With the ubiquitous use of CT scans in the emergency room setting, UPJ obstruction may be diagnosed in the workup for acute abdominal pain. Follow-up

sonogram or diuretic renogram may be near normal once the pain/obstruction has resolved consistent with the intermittent nature of UPJ blockage.

(5) MR urogram: This is another technique to diagnose UPJ obstruction. The anatomic resolution and ability to perform 3-dimensional reconstruction can localize the precise site of the obstruction as well as document the presence of a crossing vessel.

6. Treatment

a. Natural history and patient selection

(1) Symptomatic: An older child with a ureteropelvic junction obstruction may have *intermittent abdominal or flank pain*, at times associated with nausea and vomiting. Younger children tend to have more generalized lower abdominal pain, and older children will have more conventional flank pain. The pain may worsen during a brisk diuresis (after caffeine or alcohol). If the pain is intermittent, sonography should be performed during an attack of pain. If the sonogram reveals the hallmarks of a UPJ obstruction, then surgery is indicated to relieve the obstruction and consequently the pain.

Patients with a UPJ obstruction may also present with *pyelonephritis*. These patients are initially treated with antibiotics, and surgical repair of the obstruction is performed once the infection has resolved. If the pyelonephritis is acute and unresponsive to antibiotic treatment, percutaneous pyelostomy tube placement should be performed to temporarily relieve the obstruction until the infection has

resolved and pyeloplasty can be performed.

In some cases, *kidney stones* may develop in the obstructed pelvis. In this situation, whether symptomatic or not, pyelolithotomy should be performed at the same time as pyeloplasty.

In all cases, a follow-up renal ultrasound is obtained approximately 4 to 6 weeks postoperatively. If the ultrasound shows improved hydronephrosis, then the patient can be followed in the future with sonography. Follow-up MAG 3 studies are reserved for persistent postoperative hydronephrosis. Most patients (up to 95%) will have a definite improvement in the renogram and resolution of their symptoms after surgery.

(2) Asymptomatic: The asymptomatic child with an incidental UPJ obstruction poses somewhat of a management dilemma. On the one hand, some patients with an apparent UPJ obstruction will experience complete or partial resolution of the hydronephrosis without surgical intervention (transient physiologic hydronephrosis), while others will deteriorate to the point of significantly reduced renal function (a pathologic obstruction). Surgery to relieve the obstruction is necessary only in the latter group. Unfortunately, no diagnostic test alone can reliably predict which kidneys will improve and which will not. However, using the current tests available, observation and treatment protocols have been developed that minimize both the amount of unnecessary operations performed and the

number of patients who will suffer renal deterioration. There are general guidelines, and each patient's renal scan, ultrasound, and overall condition should be carefully assessed prior to making any decisions.

Observation safe: Significant hydronephrosis on ultrasound, yet renal scan reveals greater than 40% of function from the "obstructed" kidney, even if the washout is delayed.

Operate if: Significant hydronephrosis on ultrasound, and the renal scan reveals less than 40% of function from the "obstructed" kidney, especially if the washout is delayed.

b. Observation protocol: Yearly renal ultrasound and diuretic renogram should be performed until it is certain that the "obstructed" kidney's function is stabilized. The ultrasound and renogram may be performed more frequently if the patient's renal function is borderline or significant hydronephrosis is present.

c. Surgery: The success rates for open dismembered pyeloplasty are 90% to 95%. Follow-up ultrasound is obtained approximately 4 to 6 weeks postoperatively. If the ultrasound shows improvement in the hydronephrosis, then the patient can be followed safely with ultrasound at increasing intervals (initially each year, then every 2–3 years). If the postoperative sonogram has not improved, then a follow-up Lasix renogram is indicated to rule out continued obstruction. Open surgical repair remains an option; however, robot-assisted laparoscopic pyeloplasty is now routinely employed in all patients of all ages (Chapter 26).

Endopyelotomy has been used successfully in both adult and pediatric patients with UPJ.

Presently it is reserved for redo procedures.

B. **Other Causes of Hydronephrosis**

1. Congenital megaureter
    a. Definition: The presence of an enlarged ureter (greater than 7 mm diameter) with or without concomitant dilation of the upper collecting system (Fig. 14-1B).
    b. Types: Nonrefluxing, obstructed; refluxing, nonobstructed; refluxing, obstructed; nonrefluxing, nonobstructed.
    c. Pathology: The nonrefluxing, obstructed megaureter is thought to be caused by an abnormality in the distal ureteral muscle which causes an aperistaltic segment. This leads to a partial obstruction which may or may not be significant. In some cases, the ureterovesical tunnel will be abnormal as well, and urine will reflux up the ureter but be unable to come back down (refluxing, obstructed). In other cases, the urine will reflux and drain freely (refluxing, nonobstructed, see Chapter 7). Interestingly, the majority of patients will have neither reflux nor obstruction identified, yet have persistent ureteral dilation (nonrefluxing, nonobstructed).
    d. Presentation: Megaureter accounts for approximately 20% of cases of hydronephrosis in the newborn, second only to UPJ obstruction as the most common cause of hydronephrosis in the newborn. Most cases are secondary to the refluxing, nonobstructed type (see Chapter 7). The condition is mainly found incidentally on prenatal sonography, and typically the physical examination is normal, as is the urinalysis and serum creatinine. If the patients are not discovered early with prenatal sonography, they mainly present later in life with a urinary tract infection, hematuria, abdominal pain or mass, or

uremia. It is important to determine the etiology of the megaureter once discovered as many will require treatment.

e. Evaluation: The main goal is to determine which patients are obstructed, which have reflux, and which have both. The treatment options will be very different depending on the final diagnosis. The patient must have an ultrasound confirming a dilated ureter (greater than 7 mm diameter). A VCUG must then be performed to rule out reflux and to be certain there is no evidence of urethral obstruction. If there is reflux and it is severe in grade and drains poorly, *refluxing obstructed* megaureter must be considered. If there is no reflux, then the patient either has *nonrefluxing obstructed* or *nonrefluxing nonobstructed* megaureter. A diuretic renogram is then obtained to help distinguish between the two.

f. Management: The management of primary refluxing megaureter is discussed in Chapter 7. Management of obstructed and nonobstructed megaureters is discussed below; the two are distinguished mainly on the basis of symptomatology.

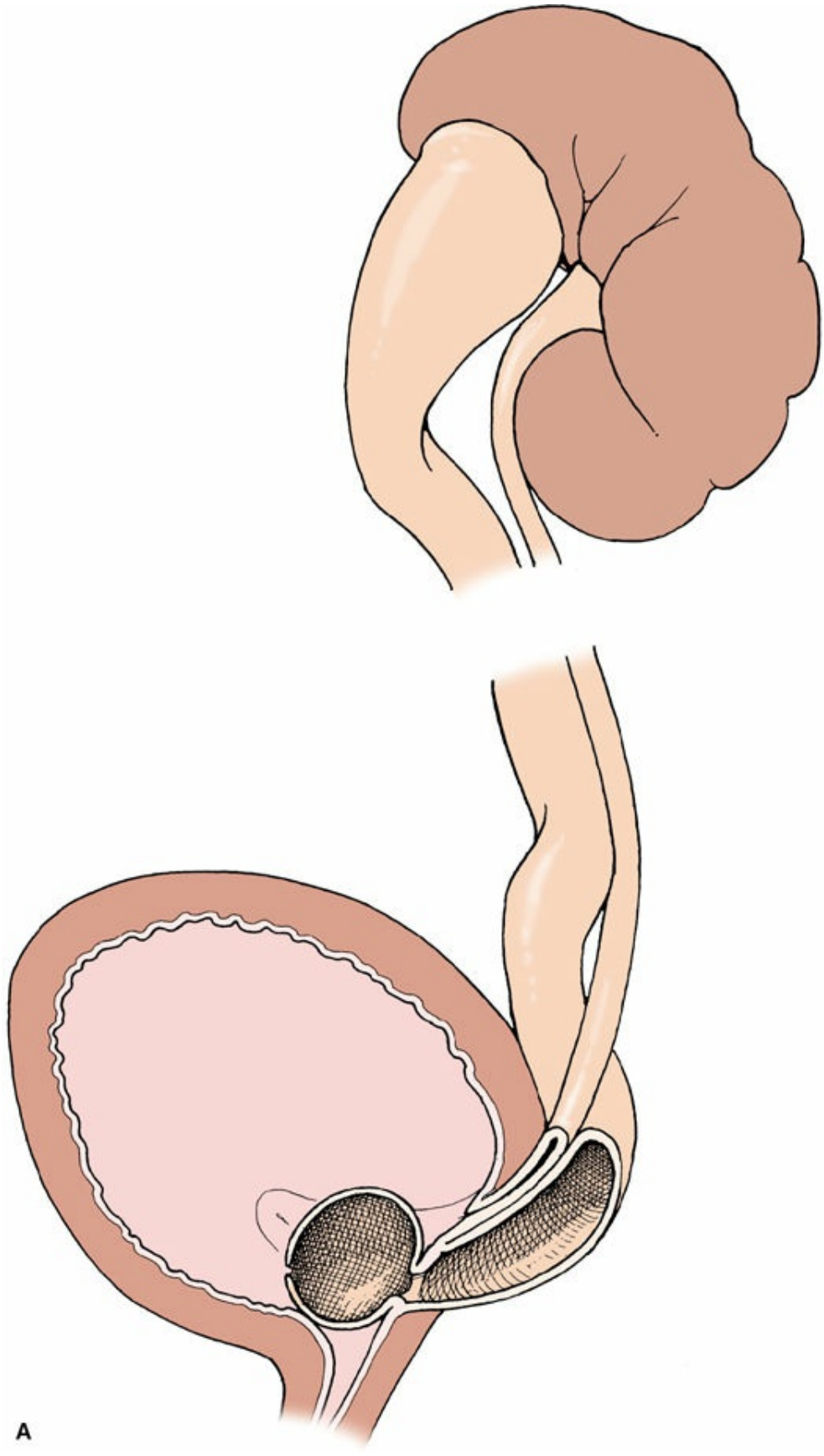
   (1) If symptomatic: The presenting signs and symptoms are usually the most important determinants as to whether surgical correction is necessary. If the child presents with recurrent urinary tract infections, pyelonephritis, persistent flank pain, or hematuria, and a megaureter is discovered, then surgical correction is warranted.

   (2) If asymptomatic: If the megaureter is discovered incidentally, and the patient has no symptoms, then nonoperative treatment is warranted as long as the function of the affected kidney is normal. This consists of

regimented surveillance with annual ultrasound. A diuretic nuclear scan is indicated to document baseline renal function. If renal function (split renal function of approximately 50% in the affected kidney and approximately 50% in the contralateral normal kidney) is normal, these patients are considered to have a *nonobstructed* system. The expectation is that with longitudinal growth over time, the congenital nonobstructed nonrefluxing megaureter will resolve. If there is an unexpected increase in hydronephrosis on ultrasound, a repeat renal scan to document lack of loss of renal function is indicated. Surgery is indicated if renal function deteriorates.

g. Surgery: If necessary, the primary obstructed megaureter can be treated surgically by excision of the distal obstructed segment, tapering of the dilated ureter and reimplantation into the bladder by a reflux prevention technique. The success rate is higher in older children, with greater risk of complications in small infants. Postoperatively, these patients are followed with renal ultrasound to document improvement in the hydronephrosis.

2. Ureteroceles
   a. Definition: A cystic dilatation of the terminal intravesical segment of the ureter (Fig. 14-3).



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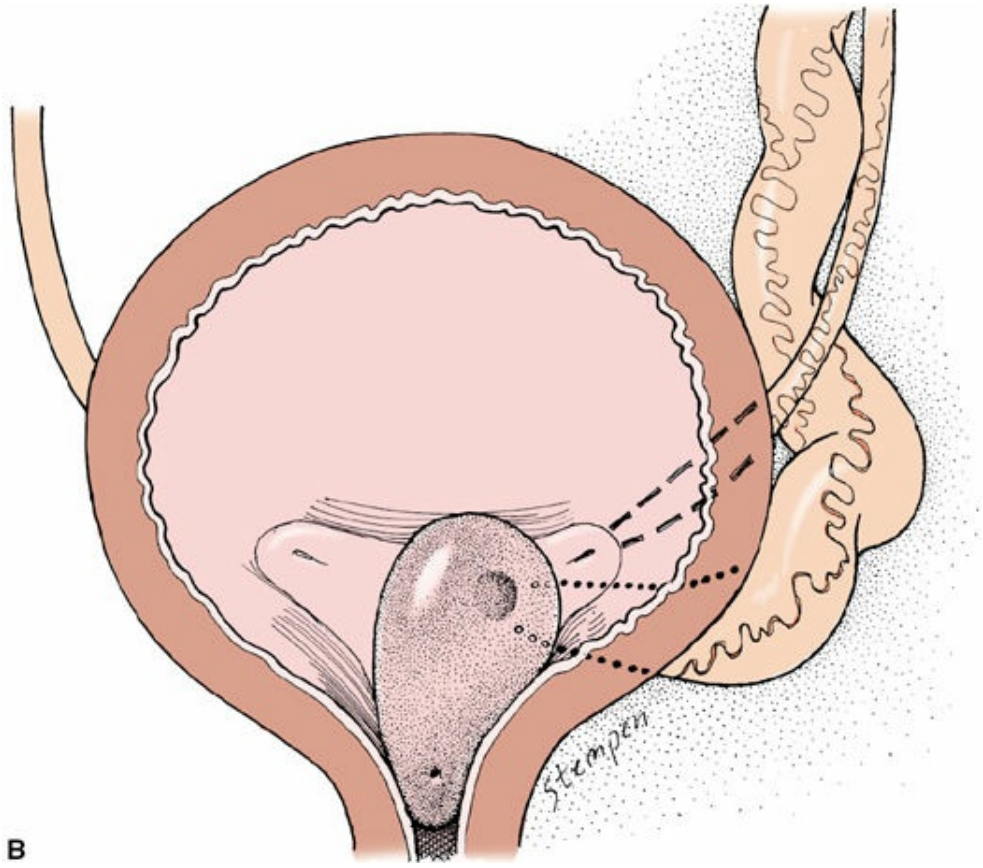


Fig. 14-3 Intravesical (A) versus ectopic (B) ureterocele

b. Incidence: It is 1 in 500 in autopsy cases. They occur 4 to 7 times more frequently in females and are more common in white patients. Ureteroceles are bilateral in 10% of cases; 80% are associated with the upper pole of a duplex system and 60% have an orifice located ectopically in the urethra.

c. Classification: Ureteroceles are classified as being either *intravesical* (within the bladder, Fig. 14-3A) or *ectopic* (some portion extends beyond the bladder neck, Fig. 14-3B). Other terms commonly encountered include *stenotic* (intravesical with a small orifice), *sphincteric* (ectopic with the orifice within the urethral sphincter), *sphincterostenotic* (same as sphincteric with a stenotic orifice), and

cecoureterocele (some part extends beyond the bladder neck, but the orifice is in the bladder).

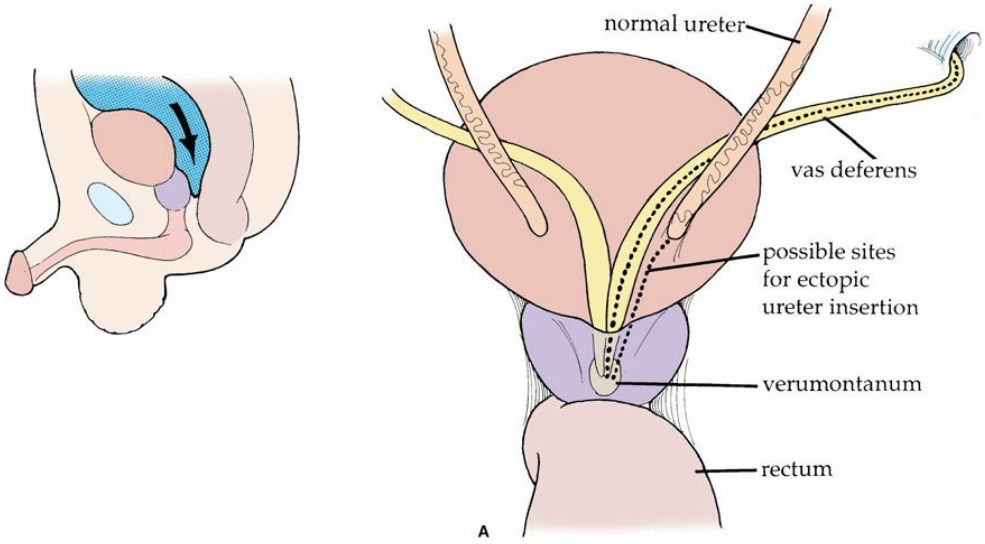
d. Presentation: The most common clinical presentation is urinary tract infection in the first few months of life. Most are now detected incidentally on antenatal ultrasonography. Some patients may have a palpable abdominal mass secondary to an obstructed kidney. Although urethral obstruction is rare, the most common cause of urethral obstruction in girls is urethral prolapse of a ureterocele.

e. Workup
   (1) Abdominal ultrasound should be performed first. This will usually reveal a well-defined cystic intravesical mass in the posterior portion of the bladder. A dilated proximal ureter may also be seen. There will most often be a duplex kidney on the ipsilateral side, and the upper pole may be dysplastic.
   (2) Renal scan is used to determine the relative function of all the renal segments.
   (3) Voiding cystourethrography (VCUG) must be performed in all patients. Up to 50% of the ipsilateral lower pole and 25% of the contralateral renal units will have vesicoureteral reflux. Also, the ureterocele can usually be seen as a round filling defect within the bladder on the initial filling films.

f. Treatment: The type of treatment depends on the type of ureterocele and the mode of presentation. Most patients will require surgery which ranges from endoscopic puncture to complete open reconstruction. If the patient presents with sepsis secondary to obstruction, then immediate drainage of the kidney is necessary. Often, endoscopic puncture of the ureterocele is the first step. This is a definitive procedure in 90%

of the cases of intravesical ureterocele, and in around 25% of ectopic ureteroceles. If endoscopic puncture fails (urinary tract infection with persistent reflux), then open reconstruction needs to be performed. If there is no function in the upper pole moiety, then upper pole nephrectomy is performed, usually laparoscopically.

3. Ectopic ureters
    a. Definition: When the ureteral orifice lies in a position caudal to the normal insertion of the ureter on the trigone, the ureter is said to be *ectopic* (Fig. 14-4).



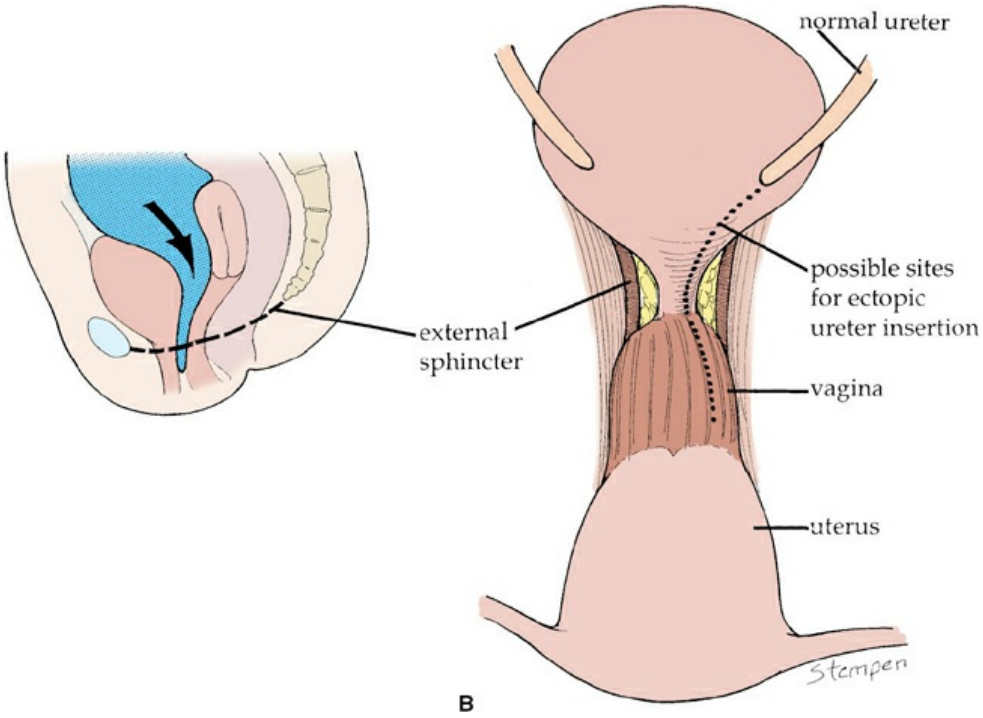


Fig. 14-4 Potential sites of an ectopic ureteral orifice. A: Male. B: Female.

b. Location of the orifice: The ectopic orifice is always along the pathway of normal development of the mesonephric system. Thus, in the male the orifice may lie in the bladder neck, prostate (to the level of the ejaculatory duct orifice), or even along the course of the male genital system, including the epididymis (Fig. 14-4A). In the female, the orifice may lie in the bladder neck, urethra, vagina, or rarely in the cervix and uterus (Fig. 14-4B).

c. Incidence: Ectopic ureters are much more common in females than in males (ratio of 6:1). Approximately 70% of ectopic ureters are associated with complete ureteral duplication. Males are more likely than females to have single system ectopia. There is a high incidence of associated renal parenchymal dysplasia in the segment drained by the ectopic ureter. Also, the incidence of contralateral duplication is as high

as 80%.

d. Presentation
   (1) In males: Usually discovered during an evaluation for urinary tract infections. Epididymo-orchitis is possible if the ureter enters the genital ducts. Males never present with incontinence since the ectopic ureter is always cephalad to the external urethral sphincter (Fig. 14-4A). Males may also present with prenatal hydronephrosis on ultrasound if the ureteral orifice is obstructed (e.g., lies within the epididymis).
   (2) In females: In infancy, girls usually present with urinary tract infection. However, older girls tend to present with incontinence. This is usually described by the parent as the child always being wet or damp even though she has normal voiding habits, or the patient becoming more wet when sitting on the parent's lap (urine pooling in the dilated ureter or vagina). Some patients may present with pyonephrosis if the ureter is extraurethral and the kidney dysplastic. Females may also present with prenatal hydronephrosis on ultrasound if the ureteral orifice is obstructed (e.g., lies within the sphincter).

e. Workup
   (1) Abdominal ultrasound should be the initial screening test. The ureter is most often dilated down to its abnormally low position.It may be followed proximally to a dysplastic or normal upper segment moiety of a duplex system. In single system ectopia, the kidney may be dysplastic and difficult to visualize.
   (2) Computed tomography (CT) scan or

magnetic resonance imaging (MRI) of the abdomen and pelvis with contrast is helpful if the ureter is not dilated (e.g., in older girls where the ureter drains into the vagina). The CT or MRI scan can usually pinpoint the location of the ectopic ureter.

(3) Voiding cystourethrogram (VCUG) should be part of the evaluation for a suspected ectopic ureter. Reflux may occur into the abnormally positioned upper segment of a duplicated system.

(4) Dye tests can be used if the above imaging studies fail to establish the diagnosis. The bladder is filled with dye, and a cotton ball is inserted into the vagina. The patient then ambulates and the ball is checked for dye.

(5) Diuretic renography is important to assess renal function, the moiety associated with the ectopic ureter. It can also show the location of an unsuspected pelvic kidney with an ectopic ureter.

(6) Cystoscopy usually does not make the diagnosis alone but can be helpful in identifying the ureteral orifice within the urethra. If the orifice is within the vagina, it is very difficult to localize on cystoscopy.

f. Management

(1) Ectopic ureter in a duplex system: Since most cases are associated with a dysplastic upper pole renal segment with minimal function, excision of this segment along with the upper pole ureter is usually curative. This can be performed laparoscopically. An alternative approach is to perform a low ureteroureterostomy reconstructing the upper pole ectopic ureter by anastomosing it to the normal lower pole

ureter. This is typically performed through a lower transverse incision or with a laparoscopic/robotic approach.

(2) Ectopic ureter in a single system: In females, the kidney associated with the ectopic ureter is usually small and poorly functional. Since the ureter inserts outside the bladder there is a hemitrigone with contralateral normal ureteral orifice. If the kidney is functional based on nuclear scan, the treatment is resection of the distal ectopic ureter and ureteral reimplantation. Otherwise laparoscopic nephroureterectomy is performed.

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15 Posterior Urethral Valves

Laurence S. Baskin

I. INTRODUCTION

Posterior urethral valves are the most common congenital cause of bladder outlet obstruction, resulting in a spectrum of damage to the entire urinary tract. Valves are obstructing membranes within the lumen of the urethra, extending from the verumontanum distally. They occur only in males (Figs. 15-1 and 15-2). They are the number one congenital cause of renal failure and renal transplantation in the pediatric population.

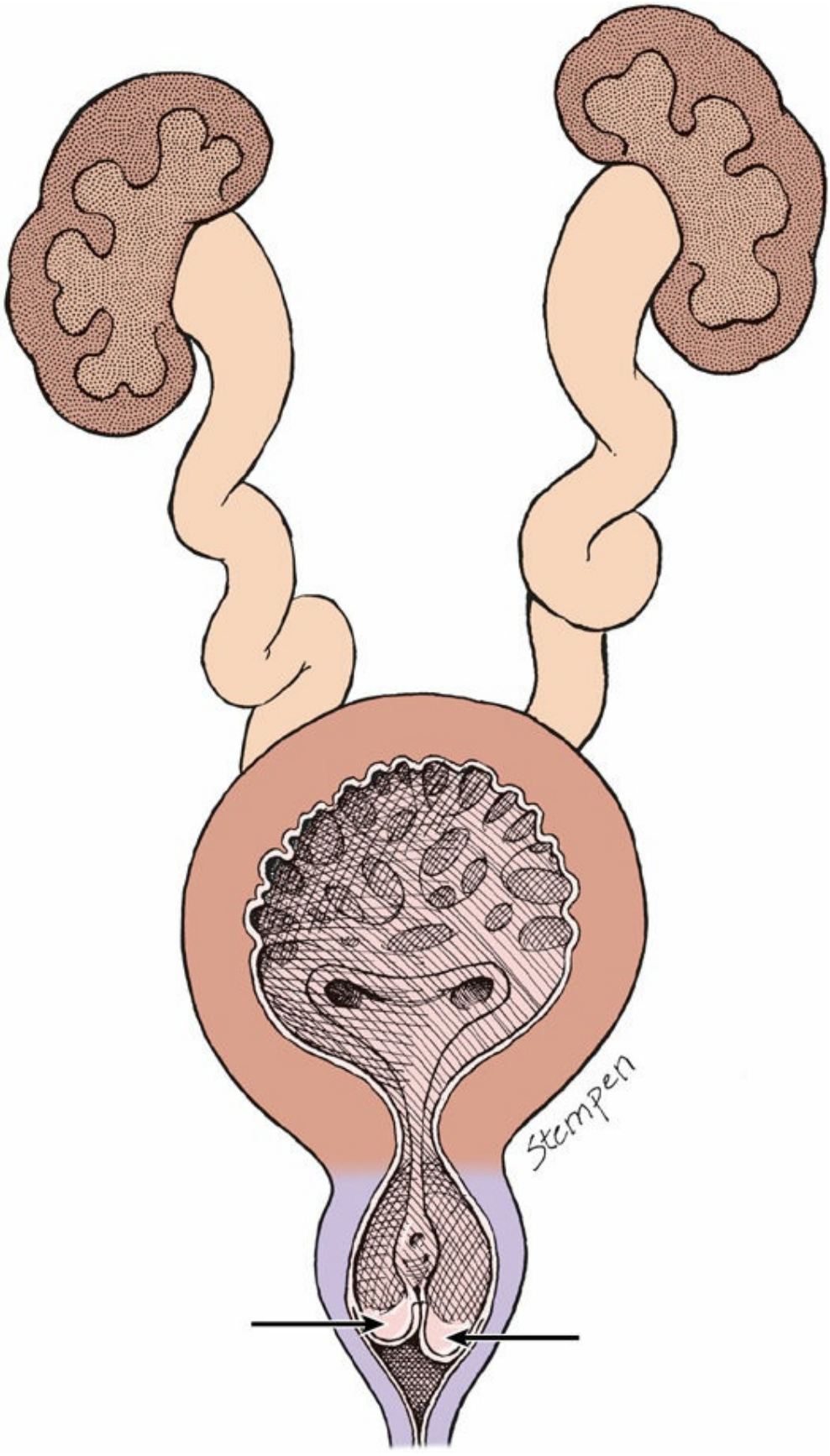
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Fig. 15-1 Schematic of posterior urethral valves. Obstructing valve is seen in the dilated posterior urethra at the bottom of the diagram (black arrows). Note the thickened bladder and bilateral hydroureteronephrosis.

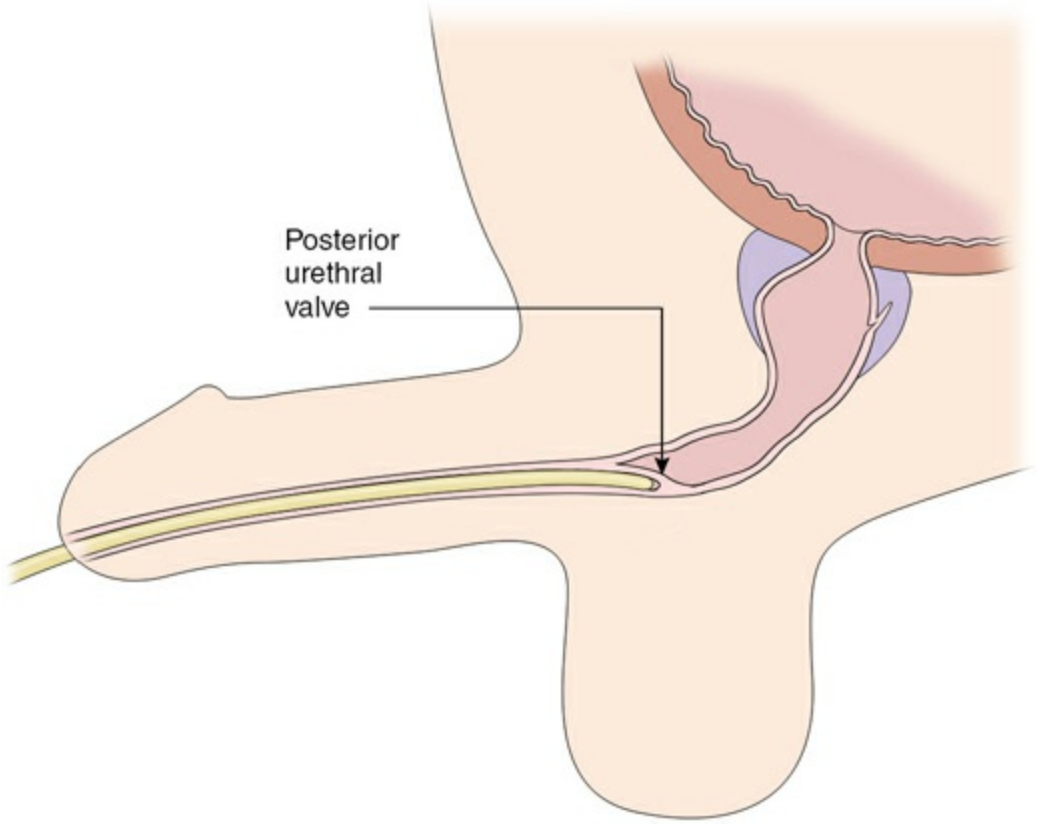


Fig. 15-2 Schematic of sagittal view of posterior urethral valve with catheter placed to the level of the obstructing valve/membrane (black arrow).

II. EPIDEMIOLOGY

A. The incidence of posterior urethral valves has been estimated to be approximately 1 per 5,000 to 8,000 male infants, although some recent studies report it to be as common as 1 in 1,250 fetal ultrasounds.
B. There does not appear to be any known ethnic or familial predisposition toward the development of valves.

III. CLINICAL PRESENTATION

The presentations of patients with posterior urethral valves display a wide clinical spectrum depending upon the degree of in utero obstruction. Patients may present prenatally or

postnatally.

A. **Prenatal Presentation**

Modern application of prenatal ultrasound examination is responsible for the detection of the majority of posterior urethral valves cases.

1. Prenatal ultrasound features
    a. Distended, thick-walled fetal bladder and a dilated posterior urethra (keyhole sign).
    b. Hydronephrosis: This can be due to bladder outlet obstruction and/or the presence of vesicoureteral reflux.
    c. Oligohydramnios: An assessment of the amniotic fluid volume is an important prognostic indicator. Since most of the amniotic fluid volume depends upon fetal urine production after 16 weeks, oligohydramnios is an indication of either poor fetal renal function or bilaterally obstructed kidneys. Severe oligohydramnios predisposes the infant to Potter's syndrome and pulmonary hypoplasia. The timing and degree of oligohydramnios play an important role in the severity of postnatal outcomes. Patients diagnosed with posterior urethral valves and oligohydramnios before 24 weeks' gestation have a poor prognosis.
2. Prenatal intervention: Prenatal diagnosis of posterior urethral valves has allowed pediatricians and pediatric urologists an opportunity to plan for and initiate treatment immediately after birth.Although some authors had expressed initial enthusiasm with in utero treatment of valves by the placement of a vesicoamniotic shunt or fetal open surgery, there is now little evidence to suggest a favorable risk to benefit ratio in terms of the preservation of renal or bladder function. Similarly, early delivery has failed to show significant benefit.

B. **Postnatal Diagnosis**

Postnatal diagnosis may occur either immediately postnatally or may be delayed several years owing to the wide spectrum of the disease and its manifestations.

1. Respiratory distress: Infants with severe oligohydramnios will usually present immediately postnatally due to the consequences of life-threatening pulmonary hypoplasia.
2. Sepsis and azotemia: The most severely affected infants may also present in the neonatal period with fulminate sepsis and azotemia, due to long-standing obstruction and renal dysplasia.
3. Abdominal distention: In the neonatal period, the presence of valves is suggested by the finding of a palpable distended bladder. The presence of urinary ascites or markedly distended upper tracts can also result in a tensely distended abdomen.
4. Voiding dysfunction: Some neonates may have difficulty in generating a normal urinary stream or fail to void during the first 48 hours of life. In rare cases, less severely affected patients may present during early childhood with incontinence or recurrent infections. Abnormalities in voiding dynamics and bladder compliance are responsible for the persistence of what is commonly called the “valve bladder syndrome,” a condition manifested by a spectrum of bladder and renal dysfunction.

IV. INITIAL MANAGEMENT OF POSTERIOR URETHRAL VALVES

Once the diagnosis of posterior urethral valves is suspected, the first step in the management often consists of the stabilization of acute illness (Fig. 15-3). The patient should be medically stabilized as much as possible before proceeding with urologic evaluation and treatment.

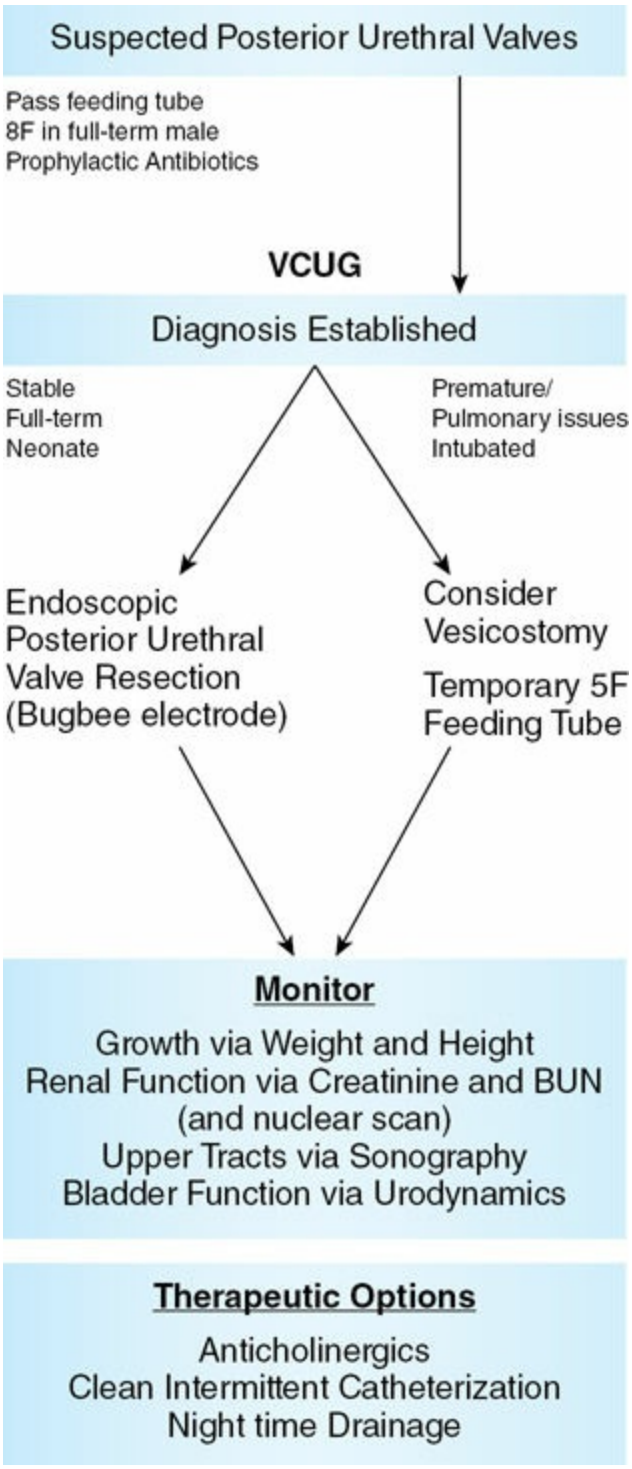


Fig. 15-3 Treatment algorithm for patients with posterior urethral valves.

A. Acute Illnesses Associated with Posterior Urethral Valves

1. Respiratory distress

2. Sepsis
3. Dehydration
4. Electrolyte abnormalities

B. Immediate urologic relief of the valve obstruction can usually be accomplished with temporary drainage of the urinary tract accomplished by placement of a pediatric feeding tube per urethra into the bladder. Foley catheters should not be used in these infants since the balloon can cause significant bladder spasms and obstruction of the ureteral orifices and hence upper tract obstruction. If the urethra is difficult to catheterize secondary to a dilated posterior urethra, the clinician should attempt to pass a Coude catheter (a curved-tip catheter), which may more easily negotiate the high bladder neck.

C. **Radiologic Evaluation of Valves**

Until an assessment of vesicoureteral reflux can be performed, the neonate should be kept on prophylactic antibiotics.

1. Voiding cystourethrogram: The diagnosis of posterior urethral valves cannot be made reliably by cystoscopy. The voiding cystourethrogram (VCUG) is considered the gold-standard examination used in the diagnosis of posterior urethral valves. Characteristic findings on VCUG include the following.
    a. A dilated, thick-walled, trabeculated bladder.
    b. An elongated, dilated prostatic urethra with a relatively narrow bladder neck.
    c. It may be possible to visualize the billowing folds of the valves as filling defects emanating from the verumontanum within the prostatic urethra.
2. Associated anomalies: The VCUG also allows identification of the numerous anomalies commonly associated with valves.
    a. Vesicoureteral reflux: Reflux has been noted in approximately one-third to one-half of patients

with valves.

b. VURD syndrome (valves, unilateral reflux, and renal dysplasia): It denotes massive unilateral reflux into a nonfunctioning dysplastic renal unit.

c. Manifestations of elevated intravesical pressure are as follows.
   (1) Bladder diverticula.
   (2) Poor bladder compliance (high pressure/trabeculated bladder).
   (3) Renal forniceal rupture, resulting in urinary ascites.

d. Pseudoresidual: Often posterior urethral valve patients have capacious upper tracts (either due to vesicoureteral reflux or high urine flow) that hold significant amounts of urine. This urine will fill the bladder after the patient voids, thereby giving the appearance of having a postvoid residual despite complete emptying.

D. **Surgical Relief of Obstruction**

Once the diagnosis of posterior urethral valves has been established with a VCUG and all acute medical issues have been stabilized, relief of the obstructing valves should be performed.

1. Primary valve ablation: In this technique, a pediatric cystoscope is carefully passed into the infant's urethra and the obstructing valves are visually identified and ablated using either a single wire or a small electrode. This approach is advocated by most pediatric urologists as the preferred treatment of valves in full-term, normal-sized infants.
2. Cutaneous vesicostomy and delayed valve ablation: Occasionally, a premature infant presents with posterior urethral valves, and because of the small caliber of the urethra, endoscopic manipulation should be avoided. A vesicostomy is performed in these infants by creating an incontinent stoma from

the dome of the bladder to the abdominal wall. This allows the urine to drain freely into the infant's diaper when the bladder pressure increases. When the infant has grown enough to allow a pediatric cystoscope to pass into his urethra, endoscopic valve ablation can be performed without excessive urethral trauma. Alternatively, valve ablation can be performed from an antegrade approach through the vesicostomy. To prevent urethral stricture and to maximize bladder potential with cycling, the vesicostomy should be closed at the time of valve ablation.

3. Temporizing upper tract diversion: Following adequate valve ablation or vesicostomy, the dilated bladder and ureters may continue to demonstrate poor peristalsis and emptying, thus predisposing the infant to urinary stasis, infection, and worsening renal function. Worsening sepsis or azotemia may be indications of poor drainage of the upper urinary tract. In these rare instances, some authors advocate temporary drainage of the upper urinary tract by performing high-loop cutaneous ureterostomy. It has been argued that upper tract diversion prevents normal cycling of the bladder, which may contribute to future voiding dysfunction. Furthermore, these infants generally have significant renal disease, requiring peritoneal dialysis and early transplantation. Most have severe reflux, and closing the ureterostomies and reconstructing these patients prior to transplantation is a major challenge, therefore upper tract diversion should be undertaken only with careful consideration. Alternatively, temporary drainage can also be accomplished with bilateral nephrostomy tubes, which can be easily removed if there is no immediate improvement. Currently, there is no clear-cut evidence that upper tract diversions improve long-term outcomes.

V. LONG-TERM MANAGEMENT OF POSTERIOR URETHRAL VALVES

Many valve patients will continue to have residual effects from bladder outlet obstruction even following definitive valve ablation. The various manifestations of bladder dysfunction together make up what is commonly referred to as the "valve bladder syndrome." It has been estimated that up to one-third of all valve patients will have significant lower urinary tract dysfunction most commonly manifested by urinary incontinence. In a small but significant number of patients, bladder dysfunction may be so severe as to lead to further deterioration of renal function. Valve patients may also have progressively poor renal concentrating ability leading to obligatory polyuria, which in turn worsens the incontinence.

A. Desired Goals in Bladder Management

1. Preservation of renal function: Serum creatinine and renal bladder ultrasound should be followed regularly.
2. Compliant low-pressure storage of urine: Urodynamic studies should be performed in patients who are failing clinically (elevated renal function, infection, increased hydronephrosis on ultrasound, or incontinence). If needed, anticholinergic medications and/or clean intermittent catheterization may be used to improve bladder function.

   Nighttime catheter drainage is also a useful technique to effectively drain the bladder and upper tracts.
3. Avoidance of infection: Vigilant investigation of fever, flank pain, or change in voiding habits is required. Some patients may require prophylactic antibiotics, especially in cases of vesicoureteral reflux.
4. Socially acceptable urinary continence: This can usually be accomplished by timed voiding habits, and

may need to be supplemented with clean intermittent catheterization and less often with surgery.

B. **Radiologic Follow-up**

Patients should be followed up with serial ultrasounds to document appropriate renal growth and hydronephrosis. All patients are recommended to have a follow-up VCUG 2 to 3 months after valve ablation to ensure that there is no residual urethral obstruction. In addition, patients with vesicoureteral reflux are typically maintained on prophylactic antibiotics and followed up with VCUG examination as needed with VCUG examinations until they demonstrate resolution of reflux, or after potty training documentation of normal bladder function. Approximately one-half of patients who initially present with reflux will have spontaneous resolution of their reflux after relief of obstruction. Another one-half can be safely maintained on chemoprophylaxis to allow for the ureters to decrease in caliber over time. On occasion, patients may have repeated complications of reflux (infection, decreased renal growth, renal function deterioration), and need more aggressive intervention including, in some cases, reimplantation.

C. **Urodynamic Evaluation**

It is of critical importance to precisely define the nature of lower tract bladder dysfunction by performing urodynamic evaluation in all valve patients who are not doing well clinically. The long-term management of valve patients will depend upon the type of bladder dysfunction exhibited on urodynamic evaluation.

D. **Medical Management**

1. Timed voiding: Poorly emptying bladders can be treated with a regimen of frequent timed voiding to reduce urinary residual and stasis.
2. Anticholinergic medications may be instituted to treat those patients who manifest low-capacity, hyperreflexic bladders on urodynamic evaluation. Close monitoring of urine output and postvoid

residual are necessary for those on anticholinergics to avoid urinary retention as these patients may be exquisitely sensitive to anticholinergic medications. If retention is suspected, the patient should be treated with clean intermittent catheterization as necessary to maintain low-pressure storage of urine.

3. Clean intermittent catheterization may be necessary to ensure complete emptying.
4. Nighttime drainage: Due to high urine output, some patients will need to use an indwelling catheter at night to allow for maximum, continuous low-pressure drainage during sleep.
5. Antibiotic prophylaxis: The persistence of vesicoureteral reflux should be treated with antibiotic prophylaxis. The decision to correct vesicoureteral reflux surgically should be considered carefully secondary to the high complication rate in these patients. If high-pressure bladders are not treated concurrently, recurrence of reflux after surgery is likely.
6. Treatment of renal insufficiency: Some children with posterior urethral valves continue to have deterioration of renal function resulting in chronic renal insufficiency. This can lead to a variety of metabolic abnormalities and growth retardation.
    a. Polyuria: Progressive decreased concentrating ability in the collecting ducts contributes to polyuria that can predispose the child to dehydration and electrolyte imbalance, especially in the face of gastrointestinal losses or fever. High urinary flow rate also causes persistent ureteral dilation and can amplify the average resting bladder pressure. The treatment of polyuria consists of timed voiding in conjunction with low renal solute load diets. Antidiuretic hormone (ADH) is not effective in treating this type of polyuria since the collecting

ducts are damaged and no longer respond to the ADH.

b. Salt-losing nephropathy: Long-term effects of obstruction of the renal tubules may result in a tubular concentrating defect and salt loss. Dietary sodium supplementation appears to be of benefit in these patients.

c. Metabolic acidosis: Metabolic acidosis enhances calcium loss from the bones and contributes to growth retardation. Dietary supplementation with bicarbonate salts should be used to correct metabolic acidosis.

d. Renal osteodystrophy: Children with chronic renal failure may require dietary restriction of phosphates or the addition of phosphate binders such as calcium carbonate to prevent bone demineralization. Calcium carbonate can also provide supplemental dietary calcium.

e. Growth retardation: Treatment involves correction of poor dietary intake and the previously mentioned metabolic abnormalities. Recombinant human growth hormone is now available to treat severely affected children.

E. **Surgical Management of Bladder Problems Related to Valves**

1. Vesicoureteral reflux: This should initially be observed for a significant period of time, and many cases will resolve on their own. However, in some cases, such as children with recurrent pyelonephritis, surgical correction of the reflux should be considered. Until resolution of the reflux is accomplished, the child should remain on prophylactic antibiotics. Prior to correction of vesicoureteral reflux, care must be taken to ensure that the patient voids regularly and to completion, since the correction of the reflux will be compromised by a high-pressure bladder. In the

presence of high bladder pressures, the ureter may be recruited to act as a pop-off valve, which would compromise the anti-reflux mechanism further.

2. Bladder augmentation: In cases of children with severely contracted small-capacity bladders that fail to respond to maximal medical therapy, it may be necessary to surgically augment the bladder in order to achieve appropriate bladder capacity and urinary continence, and to preserve renal function. Surgical bladder augmentation is usually performed using a detubularized segment of ileum as a patch on the dome of the bladder. Patients with bladder augmentation often require clean intermittent catheterization for bladder emptying. They are at risk for mucus in the urine which can lead to urinary tract infections and bladder stones. They are also at risk for bladder perforation which can be lethal secondary to unrecognized source of sepsis. In the long term, there may also be an increased risk of malignancy necessitating long-term follow-up in these patients. Thus bladder augmentation is prone to additional complications and the decision to proceed to augmentation in these patients should not be taken lightly.

VI. SUMMARY

Posterior urethral valves are one of the most common urologic perinatal emergencies. The immediate survival of the infant depends upon early recognition and stabilization of the acute metabolic abnormalities. Following relief of the obstructing lesion, patients with posterior urethral valves often continue to manifest a variety of urologic dysfunction related to abnormal bladder function, and should be closely followed throughout childhood. Accurate characterization by urodynamic studies and careful management of bladder dysfunction are the keys to the long-term prognosis of these patients.

RECOMMENDED READING

McAninch J. Disorders of the penis and urethra. In: Jack McAninch and Tom Lue *Smith and Tanagho's GeneralUrology, 18th ed.* New York: McGraw Hill; 2013.

Shula A. *Posterior urethral valves and urethral anomalies. In:* Kavoussi LR, Novick AC, Partin AW, Peters CA, Wein AJ, eds. *Campbell-Walsh Urology, 11th ed.* Philadelphia, PA: W.B. Saunders; *2016:540*.

16 Congenital Anomalies: Urachal Anomalies, Exstrophy-Epispadias Complex, Imperforate Anus, Cloaca, and Prune Belly Syndrome

Joseph Borer

I. URACHAL ANOMALIES

See Figure 16-1.

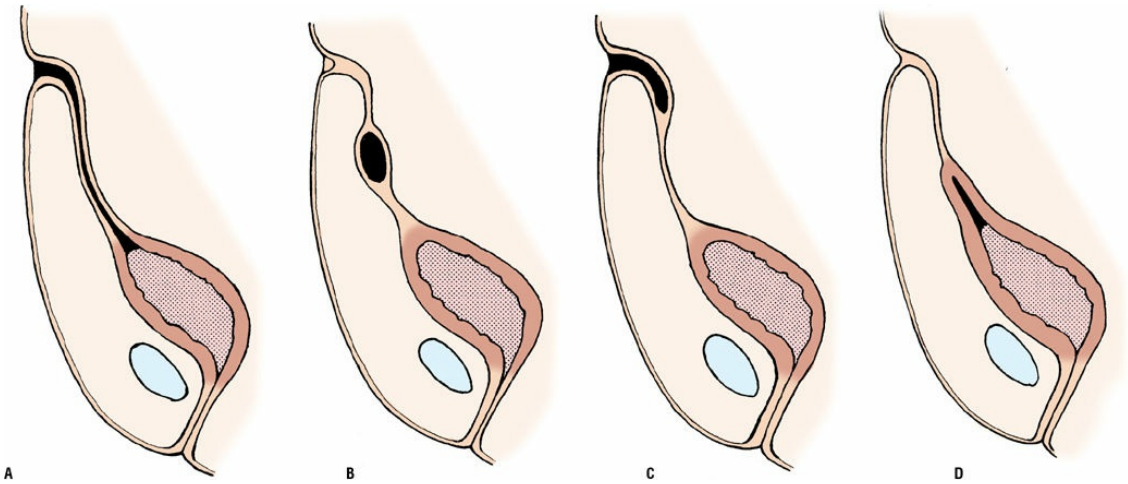


Fig. 16-1 Urachal anomalies. A: Patent urachus. B: Urachal cyst. C: Urachal sinus. D: Urachal diverticulum.

A. Background

The urachus is a fibrous band of tissue that extends from the dome of the bladder to the umbilicus as the remnant of the allantoic duct. Ordinarily, this tract obliterates by the end of the first trimester, but rarely it remains partially or completely patent.

B. Presentation

Complete failure of urachal obliteration may result in a persistent patent communication from the bladder to the umbilicus with either constant or intermittent leakage of urine or mucus. Although this may occur as a result of bladder outlet obstruction such as posterior urethral valves, more often there is no associated anomaly. The usual presentation is in the neonate with constant or intermittent moisture/drainage from the umbilicus that may worsen during crying or straining. If the urachal lumen is only partially obliterated, it may present later in childhood with enlargement due to accumulation of desquamated products or infection. Signs and symptoms may include pain, fever, mass, umbilical drainage, and in some cases signs of urinary tract infection (UTI) such as urinary frequency, urgency, and dysuria. Included in the differential diagnosis of such a presentation are infected urachal cyst, urachal sinus, or urachal diverticulum, vitelline cyst, umbilical hernia, and ovarian cyst. Often there is an associated UTI if the urachal remnant is in communication with the bladder.

C. **Workup**

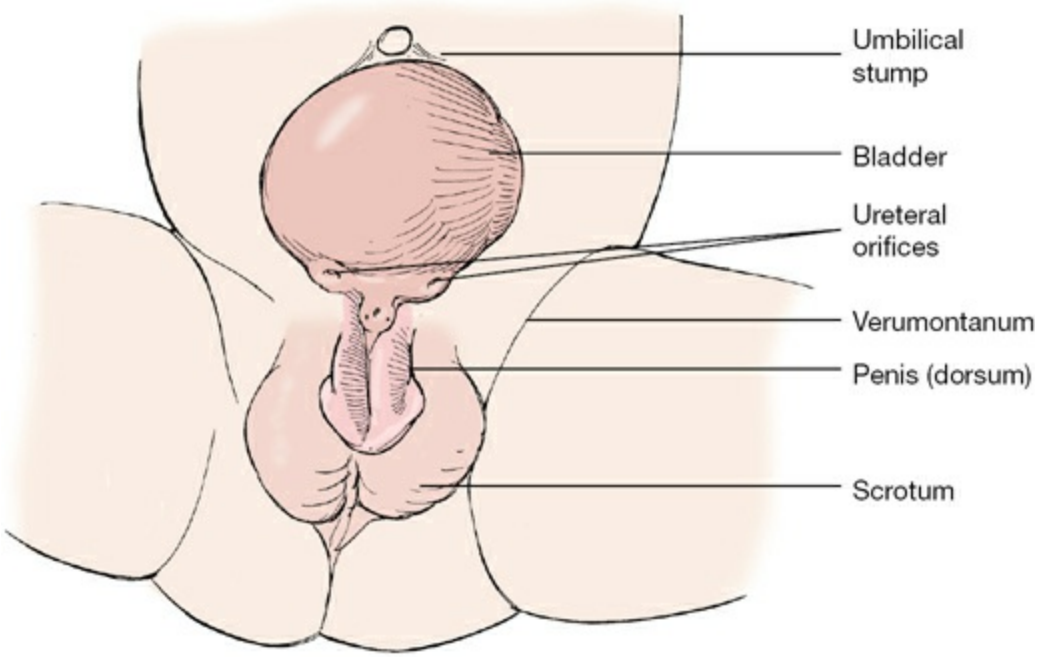
If one suspects a urachal anomaly by history and/or physical examination, an ultrasound of the abdomen with particular attention to the abdominal wall may be diagnostic. Other forms of urachal anomalies may require placement of a probe into the urachal tract or instillation of contrast for a fluoroscopic fistulogram. Occasionally, a voiding cystourethrogram (VCUG) will delineate the communication. However, the VCUG is typically more useful for evaluating potential associated lower urinary tract anomalies.

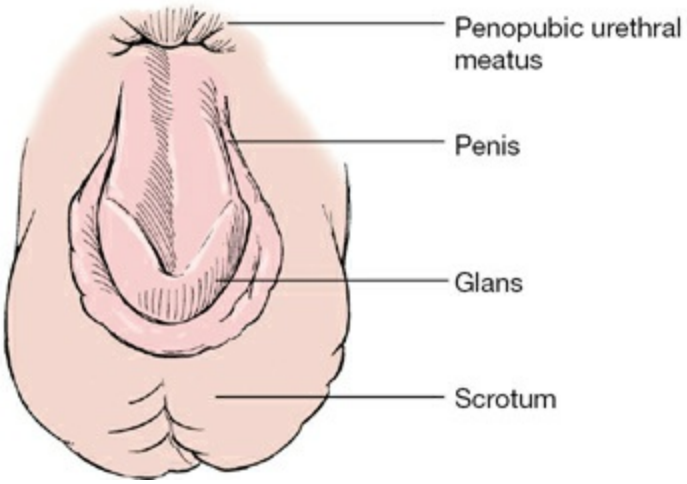
D. **Treatment**

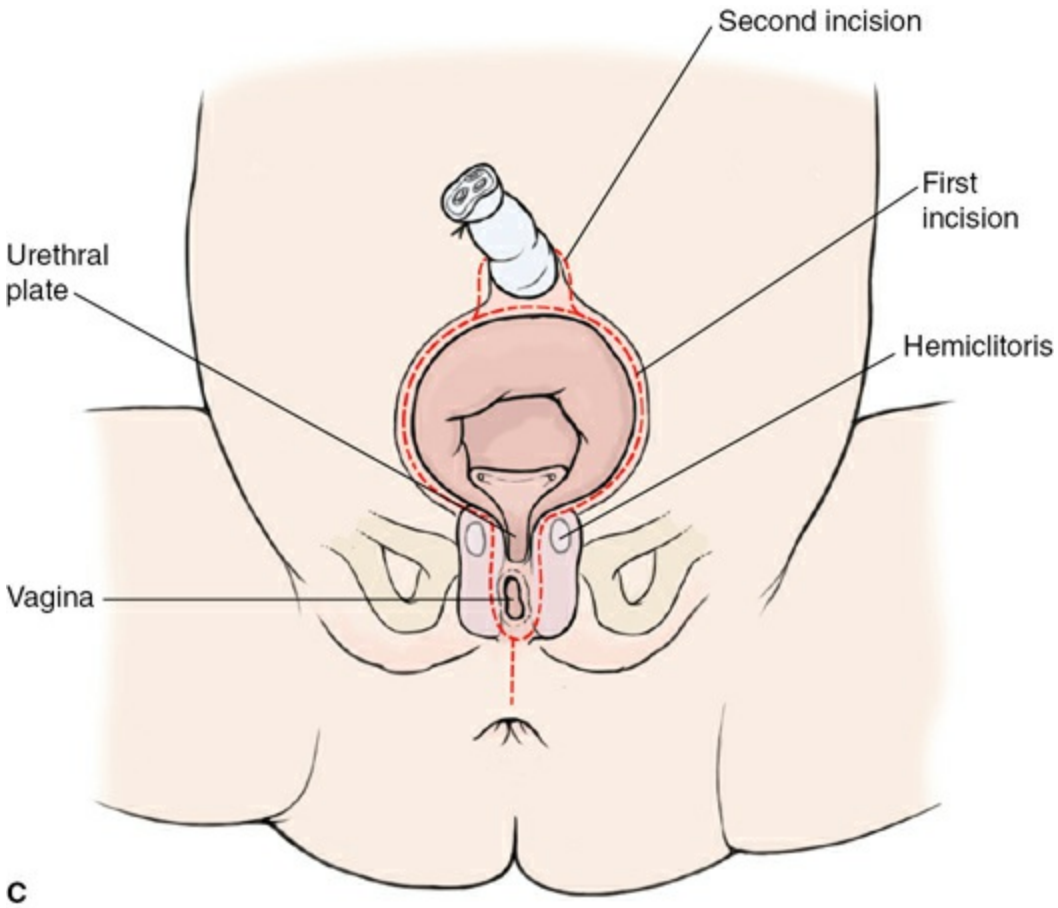
Complete extraperitoneal excision of the urachal malformation is indicated in most cases. Occasionally, infected cysts may benefit from percutaneous drainage and antibiotic therapy in the acute setting. However, definitive management requires resection because of the

high likelihood of recurrence. Although adenocarcinoma of the urachus is rare, it has been reported to arise in patients with a history of infected cysts. For this reason, it is recommended to resect a “cuff” of surrounding bladder tissue during excision of any urachal abnormality.

II. EXSTROPHY-EPISPADIAS COMPLEX






Second incision
First incision
Urethral plate
Hemiclitoris
Vagina

C

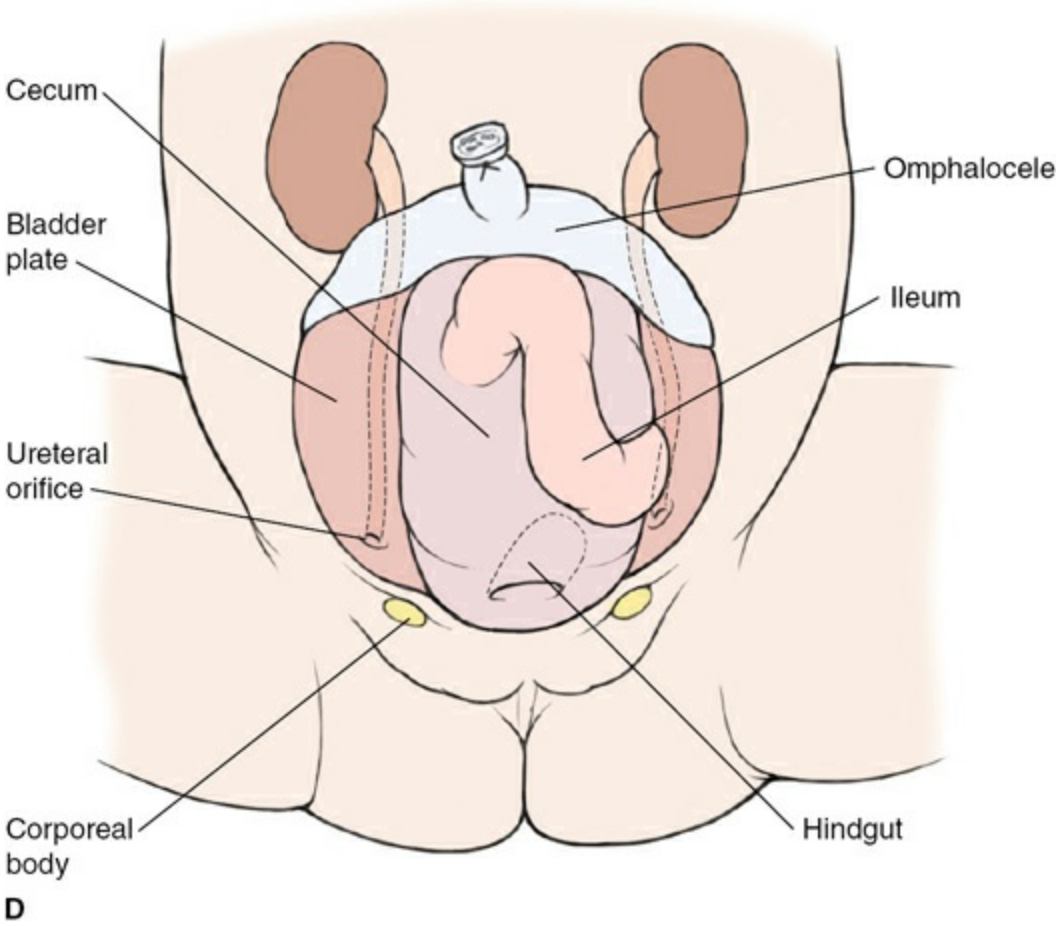


Fig. 16-2 A: Exstrophy-epispadias complex. B: Epispadias, penopubic (boy). C: Bladder exstrophy (girl). D: Cloacal exstrophy (boy).

A. Background

The exstrophy-epispadias complex is a spectrum of anomalies with many similarities, but varying degrees of severity (Fig. 16-2). Within this spectrum, severity and complexity increases from epispadias to bladderexstrophy to cloacal exstrophy. Bladder exstrophy is seen in approximately 1 in every 30,000 to 40,000 births, and is more common in boys. Within the exstrophy-epispadias spectrum, bladder exstrophy occurs in 60% of patients, epispadias (all forms) in 30%, and cloacal exstrophy and other variants in 10%.

B. Embryogenesis

The most popular theory suggests overdevelopment of a normal structure known as the cloacal membrane which is

present during early fetal development, but abnormally persists beyond the 4th week of gestation, preventing the lateral mesoderm from migrating medially. Once the membrane disappears by the 9th week, the internal surface of the bladder is exposed on the lower abdominal wall with the umbilicus in abnormally low position adjacent to the cephalad apex of the bladder. There is also failure of urethral tubularization. In the most severe form, cloacal exstrophy, an abnormally large cloacal membrane perforates prior to division of the cloaca itself by the urorectal septum. This results in exstrophied bladder halves that are separated by an interposed exstrophied ileocecal bowel segment.

C. **Anatomy**

For individuals with bladder exstrophy, the inner surface of the urinary bladder is open and exposed on the lower abdominal wall. The bladder is not covered as normal by abdominal wall muscle, fascia, and skin, but rather the bladder is essentially inside out with the inner surface exposed. The disorder usually involves several organ systems including the urinary tract, reproductive tract, digestive system, muscles and the skin of the lower abdominal wall, and the muscles and bones of the pelvis. In addition, the inner lining of the urethra is also exposed on the dorsal surface of the penis in boys or between the separated right and left halves of the clitoris in girls. The failure of the urethra to close normally and its exposure on the surface is called epispadias. Epispadias is a consistent component of bladder exstrophy, but may also present in isolation (open, exposed urethra with closed bladder). In the absence of normal closure of the bladder and urethra, the bladder lacks the ability to store urine, and urine constantly trickles onto the exposed inner surface of the bladder and surrounding skin.

Bladder exstrophy and cloacal exstrophy may be diagnosed prenatally by an experienced ultrasonographer, or at birth as the exposed bladder and urethra (and bowel

as well in cloacal exstrophy) are obvious malformations. The bladder plate may vary in size from a small vestigial structure to 6 cm to 7 cm in diameter. Pubic bone separation from the anterior midline (pubic diastasis) is present in all cases. The upper urinary tracts are generally normal except in cloacal exstrophy patients of whom up to two-thirds may have abnormalities such as renal ectopia, dysplasia, or agenesis. Exposure of the bladder results in bacterial colonization, and may result in squamous metaplasia along the edge of the bladder bordering skin. Once the bladder has been closed, vesicoureteral reflux (VUR) occurs in the vast majority of patients due to the abnormal insertion of the ureters and lack of muscular backing and thus lack of the normal anti-reflux flap-valve mechanism. Inguinal hernias are common, especially in boys. The testes are descended normally in most cases. Infrequently, rectal prolapse may be present due to weakness in the perineal floor and the anterior aspect of the levator muscle complex.

D. **Initial Management and Evaluation**

1. Soon after initial plastic clamp occlusion of the umbilical cord at delivery, the clamp should be exchanged for soft cloth “umbilical tape” or silk ligature to limit trauma to the exposed mucosal surface of the bladder. The bladder and urethra may be covered with a transparent adhesive dressing (“Saran wrap”) that adheres to the intact skin immediately surrounding the exposed bladder, but glides over and protects the exposed mucosa. This allows free egress of urine from the ureteral orifices on the bladder surface and subsequent passage caudally along the genitalia and into a diaper. Touching the bladder mucosa and potential abrasion should be avoided.
2. Initial evaluation includes a complete blood count, serum electrolytes, blood urea nitrogen, and plasma creatinine. In general, patients with epispadias or

bladder exstrophy have normal kidneys and normal renal function, whereas abnormalities in renal number, position, and function are common in cloacal exstrophy. Imaging studies include renal ultrasound to screen for any congenital anomaly of the kidney or urinary tract. Abdominal plain film is helpful for measuring the degree of pubic diastasis.

E. **Initial Surgical Management**

There are several different approaches to initial repair for the boy or girl with bladder exstrophy. Variation in management may exist per institution and/or surgeon for either timing and/or technique of initial and definitive repair of bladder exstrophy. With regard to timing, the initial reconstructive surgery may be performed within the first 2 to 3 days of life (immediate) or at approximately 6 to 8 weeks of age (delayed). Delaying the initial closure may be the preference of some pediatric urologists based on practice or based on the specific anatomy of the individual patient. Examples of this would be delaying initial surgery if the bladder or genitalia was too small for safe repair and/or if the baby was born prematurely. Regarding variation in technical approach to initial repair, of bladder exstrophy there are several options: (1) modern staged repair of exstrophy (MSRE), (2) complete primary repair of exstrophy (CPRE), (3) soft tissue reconstruction, and (4) urinary diversion.

1. Modern staged repair of exstrophy

   Stage 1: Initial closure: During this first stage, the bladder, proximal urethra (in the boy), and abdominal wall are closed, the umbilicus is reconstructed, and an incision in the pelvic bones (osteotomy) is sometimes performed to aid in the repair. Whether or not the infant needs an osteotomy is dependent on how soon after birth the closure is performed, the degree of pubic diastasis, and flexibility of the pubic bones. Most include osteotomies with closure for a baby older than 72 hours of age.

After surgery, the baby will be placed with the lower abdomen, pelvis, and legs in traction/splint in order to stabilize the pelvis and repair as an aid to healing. Patients may stay in the hospital for 1 to 4 weeks and will be carefully observed during this time. Antibiotics are given during and after the surgery to decrease the risk of infection. The bladder is drained continuously with a suprapubic cystostomy tube and removed approximately 4 weeks following surgery provided VCUG and voiding efficiency are satisfactory.

Stage 2: Epispadias repair: Epispadias is a congenital defect wherein the urethra fails to close. Epispadias is always associated with bladder exstrophy. In boys, the distal exposed urethra, purposely not repaired at the first stage, is now closed at the second stage of the MSRE. In girls, the urethra is usually closed along its entire length at the first stage of MSRE, extending all the way from the bladder to the surface of the introitus between the labia to end in normal position. The surgical procedure used to correct epispadias in boys aims to complete the reconstruction of the urethra with urethral meatus on the glans and restore the appearance of the external genitalia to normal. This repair is performed at approximately 6 months of age.

Stage 3: Bladder neck reconstruction: Bladder neck reconstruction (BNR) represents the third and final stage of the modern staged approach. Bilateral ureteral reimplantation is almost always performed with BNR. Performance of this stage of the MSRE depends on sufficient growth of the bladder as judged by bladder capacity. BNR is usually performed between the ages of 4 and 8 years.

2. Complete primary repair of bladder exstrophy: With advances in surgical technique, the initial surgery for

children with bladder exstrophy may combine the first two stages of the MSRE, that is, closure of the bladder and epispadias repair at the same setting, and is called complete primary repair of bladder exstrophy (CPRE). This technique combines the goals of the first two stages of the staged reconstruction into a single operation in order to create an environment that allows more normal bladder function (cycling) to begin earlier, optimizing bladder growth and development. In some boys and more often in girls, successful CPRE may eliminate the need for BNR later in life.

The operation consists of closure and internalization of the bladder, closure of the urethra (epispadias repair), repair of external genitalia, and repair/approximation of the lower abdominal wall muscles and skin. Some newborns may require osteotomy in order to help bring the pelvic bones closer together. This approach has resulted in adequate urinary continence in some patients, therefore making it unnecessary to perform formal BNR to treat incontinence. Regardless of the outcome of continence, almost all boys and girls with bladder exstrophy will require surgery for treatment of vesicoureteral reflux, which is present in nearly all babies with bladder exstrophy. All of these babies require traction in order to stabilize the repair and optimize healing following initial repair.

Complete primary repair may be delayed and performed at approximately 6 to 8 weeks of life with the addition of a bilateral pelvic bone osteotomy. It is felt by some that delaying CPRE beyond the first 2 to 3 days of life has several advantages for the child and the family unit. It presents an opportunity for normal bonding between the baby and parents before the initial reconstructive surgery and lengthy recovery period that follows. This time between birth and

initial repair will allow for growth, development, and additional maturation of some organs and systems prior to the complex surgery, and will make the anesthesia and the surgery safer.

3. Soft tissue reconstruction: The soft tissue reconstruction/mobilization technique involves two stages. Initial bladder closure similar to that in the first stage of the MSRE is performed in the newborn with or without osteotomy. The second stage involves bilateral ureteral reimplantation, bladder neck reconstruction/ tubularization, epispadias repair, and freeing of the neurovascular bundle proximal to the pudendal pedicle. Dissection under the periosteum provides a delicate but safe plane to the experienced surgeon for freeing of the neurovascular bundle and is felt to gain length on the phallus.
4. Urinary diversion: This strategy for management, applied in some institutions, involves creating a purposeful and functional connection between the urinary and intestinal tracts. Although there are several variations on this theme, basically the urine is diverted (directed away) from the urinary bladder and into the bowel (large intestine/colon) for temporary storage and then intermittent emptying per rectum with the stool. Passage at regular intervals is under the control of the child. The bladder and urethra are closed, but are “dry” and are neither exposed to the urine nor necessary as a conduit for the urine.

F. **Epispadias**

Epispadias is isolated incomplete closure of the urethra and is rarer than bladder exstrophy. The most common form of epispadias in boys is called penopubic epispadias, in which the site of the urethral opening is at the dorsal base of the penis. More uncommon variations may exist in boys, including opening of the urethra on the penile shaft, or the rarest, glanular epispadias. In general, the more proximal the meatus, the more likely the presence of

pubic diastasis, and maldevelopment of the external urethral sphincter and bladder neck continence mechanisms. Repair of epispadias is performed as discussed per bladder exstrophy closure, and can be done in the newborn or within the first few months of life. In some boys with penopubic epispadias, wide pubic diastasis, and a patulous bladder neck, the surgical correction of incontinence may be performed at the time of epispadias repair.

G. **Cloacal Exstrophy**

In the past, patients with this most severe and rare form (incidence of 1 in 200,000 to 400,000 live births) of the exstrophy-epispadias complex were typically given supportive care only. Associated abnormalities include omphalocele, numerous gastrointestinal anomalies including malrotation, duplication, duodenal atresia, short-gut syndrome, and Meckel's diverticulum, and significant genitourinary anomalies including separate bladder halves and bifid genitalia. Urology, orthopedics, neurosurgery, anesthesia disciplines, and social services should be consulted. In the past, newborn males were, in some instances, gender converted to female as a result of inadequate development of the genitalia and the poor prognosis for developing a normal male phenotype. Gender conversion is infrequent in contemporary management of cloacal exstrophy. Girls with cloacal exstrophy will often have müllerian abnormalities such as duplication of the internal female reproductive organs.

With modern surgical techniques and a multidisciplinary approach to care, children with this complex disorder can achieve acceptable lifestyles in their genotypic gender. Following initial evaluation and stabilization of the newborn, surgical management is often a staged approach with the initial surgery in the newborn focused on safety and functionality. The cecal plate and prolapsed ileum interposed between the bladder halves is separated from the bladder and urinary tract. The

prolapsed ileum is reduced, the cecal plate is tubularized, and the hindgut (distal colon) is brought out to the skin in the left lower quadrant of the abdomen as a functional end-colostomy. The medial edges of each hemibladder are then approximated in the midline. This closure of only the posterior wall of the exposed (exstrophied) bladder essentially converts cloacal exstrophy to classic bladder exstrophy. At a later time, with the help of osteotomies, the bladder exstrophy can then be repaired in either a staged or complete repair technique. In some instances, complete repair can be performed in the newborn.

III. IMPERFORATE ANUS

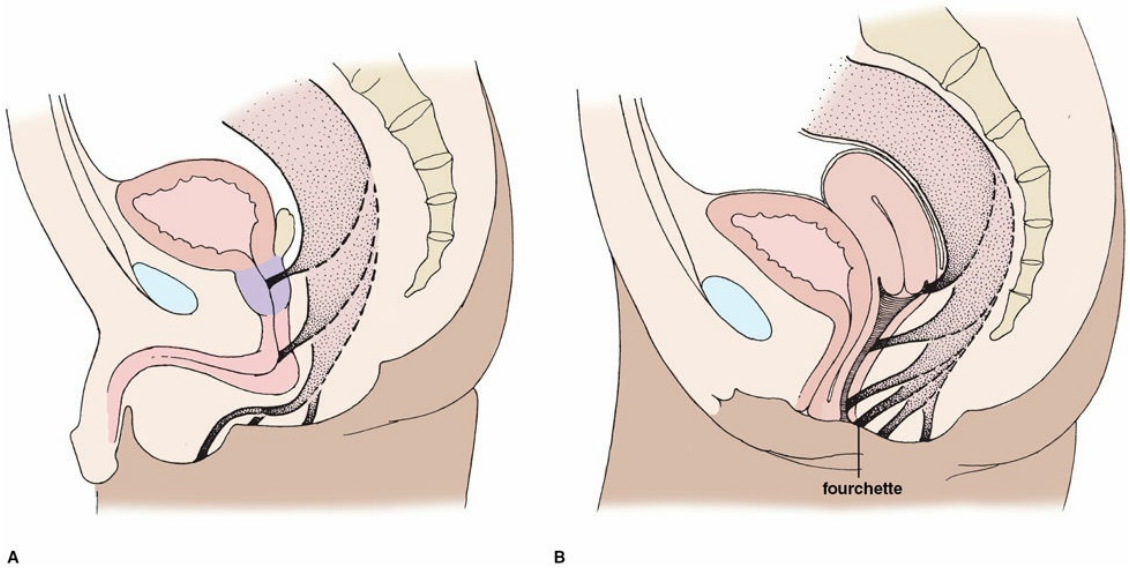


Fig. 16-3 Imperforate anus. A: Boys. B: Girls.

A. Background

Imperforate anus comprises a spectrum of anorectal anomalies ranging from simple anal fistula to complex malformations involving multiple organ systems (Fig. 16-3).

1. Associated anomalies are seen in up to 50% of cases and urologic involvement in 26% to 50%. Generally, the more severe the defect (i.e.,the higher the rectourethral or rectovaginal communication), the

higher the incidence of associated anomalies.

a. VACTERL association: Previously known as VATER (*v*ertebral, *a*norectal, *t*racheo-*e*sophageal fistula, *r*adial abnormalities), the terminology has been updated to include *c*ardiac, *r*enal, and *l*imb anomalies. Spinal abnormalities include hemivertebra, sacral agenesis or deformation, and spinal dysraphism (spina bifida).
b. Genitourinary anomalies: Major malformations include renal agenesis (20%), vesicoureteral reflux (23%), hydroureter (12%), neurogenic bladder (6%), cystic or dysplastic kidney (5%), renal ectopia (5%), ureteral ectopia (4%), and ureteropelvic junction obstruction (3%). Minor malformations include cryptorchidism (4%), ureteral duplication (3%), hypospadias (3%), and renal malrotation (2%).

2. Embryology: By the 8th week of gestation, the primitive hindgut becomes separated into the rectum and the urogenital sinus by the descending urorectal septum. Incomplete migration of the septum with persistence of the cloacal membrane may result in communication (fistula) between the rectum and the urinary tract as well as malformations of the pelvic musculature (sphincter).
3. Classification: Anorectal anomalies can be divided into high, intermediate, or low defects based on the level of the fistula between the rectum and the urinary tract or the level of the rectal agenesis.
4. Morbidity: Factors contributing to morbidity in these patients relate mainly to genitourinary (GU) anomalies, spinal (especially sacral) anomalies, other malformations, and the quality of bowel and urinary sphincters. GU factors include sepsis, absorptive hyperchloremic metabolic acidosis (from absorbed urinary electrolytes via the bowel mucosa),

progressive pyelonephritic scarring exacerbated by vesicoureteral reflux, neurologic bladder dysfunction, and urethral obstruction.

B. **Prenatal Diagnosis**

Although a subtle finding on ultrasound, a dilated distal bowel segment can be a tip-off. Occasionally, intralumenal calcification is present which occurs as a result of mixed stagnant urine and meconium.

C. **Diagnosis and Management**

1. Perineal inspection: The initial evaluation of the perineum will yield much information about the severity of the defect and the type of intervention necessary for the infant. In males, addition of a urinalysis to assess for meconium will determine whether a colostomy is needed. If there is any question regarding the diagnosis, a cross-table lateral plain X-ray with the patient in the head-down position and with skin marker at the level of the anus (or where it should be) should be done (invertogram).
2. Surgical management: Most patients with high lesions will require a colostomy to divert the fecal stream temporarily until a more definitive repair is accomplished. Definitive repair is most often performed with the posterior sagittal anorectoplasty (PSARP) and repair/closure of the rectourinary fistula. The posterior approach is advantageous in preserving the sphincteric musculature including the puborectalis sling portion of the levator muscles. In lower or more minor lesions, a posterior anorectoplasty may accomplish the job without having to temporarily divert stool with a colostomy.
3. Urodynamics: Urodynamic evaluation is an important part of management because of the possibility of spinal dysraphism or sacral agenesis, and/or operative injury to bladder, and/or colonic innervation.
4. Urologic interventions

a. Antibiotic prophylaxis: Until lower urinary tract anomalies are ruled out or reconstructed, all patients should be placed on prophylactic antibiotics to decrease the risk of urosepsis.

b. Catheterization difficulties: In some boys, repair of the fistula results in urethral narrowing, scarring, or possibly the presence of a diverticulum all of which make catheterization a challenge. Use of a curved (coudé) tip catheter may be helpful. If a patient is unable to negotiate the urethra with any catheter and requires intermittent catheterization, placement of a continent catheterizable channel to the bladder (Mitrofanoff/appendicovesicostomy) may be a suitable alternative.

c. Augmentation cystoplasty: If bowel segments are necessary to enlarge the capacity of the bladder, one should avoid using the sigmoid colon so as to not devascularize the distal bowel. Also the ileocecal valve should be preserved to avoid exacerbating stool incontinence in the presence of marginal sphincteric function.

IV. CLOACA

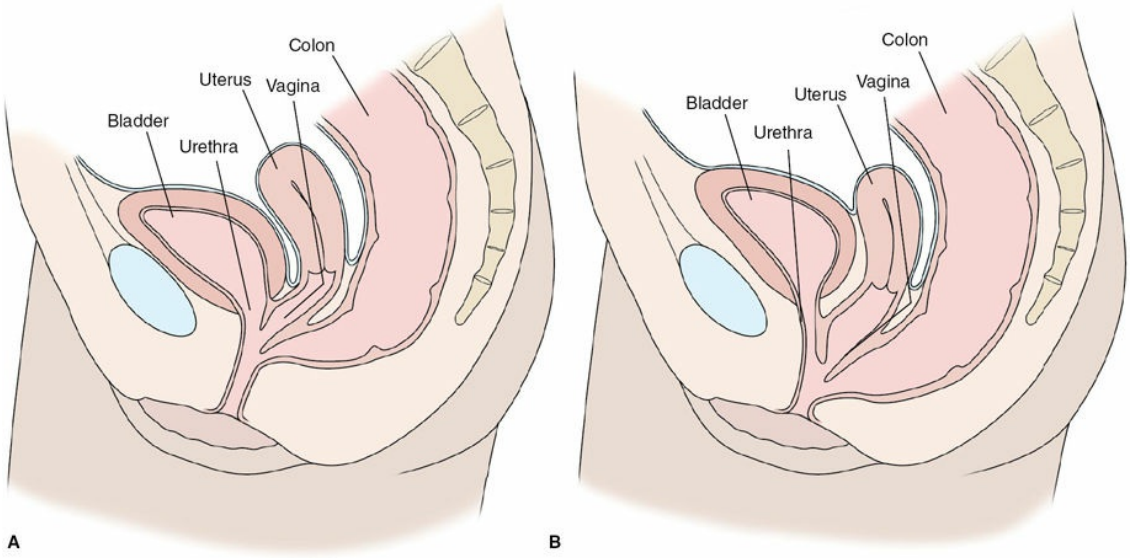


Fig. 16-4 Cloaca. (A) high confluence further from skln (B) low confluence closer to the skin.

A. Background

Cloaca is a malformation in the female wherein the urinary, genital, and gastrointestinal tracts exit the body as a single opening (common channel) (see Fig. 16-4). It is also referred to as cloacal malformation or persistent cloaca. Cloaca occurs in approximately 1 per 50,000 live female births. Deformities encompass a wide range of defects involving multiple organ systems. The most pronounced effects are in the intestinal and genitourinary tracts, raising concerns about urinary control, bowel control, and sexual function. Patients are often grouped based on the level of the confluence of the urinary, reproductive, and gastrointestinal tracts. A "high confluence" refers to the joining of these three systems relatively deep to the surface, with a long common channel terminating in a single opening on the perineal surface (see Fig. 16-4A). "Low confluence" refers to those girls with a relatively superficial confluence and a short common cloaca channel (see Fig. 16-4B).

B. Associated Anomalies

Associated anomalies are seen in up to 50% of cases. In general, the more severe the defect the deeper the confluence, and therefore, the longer the common channel and the higher the incidence of associated anomalies. Tracheoesophageal fistula and esophageal atresia are common associated abnormalities. Abnormalities of the spinal column, the bones in the pelvis, lower spine, or sacrum are common. These include hemivertebra, sacral agenesis or deformation, and spinal dysraphism. Spinal cord abnormalities are seen in approximately one-third of patients. Open spinal cord defects such as those seen in the spina bifida population are uncommon. In more complex patients, cloaca may be the anorectal component of the VACTERL association (see Section III, imperforate anus). These patients require multidisciplinary evaluation

and care.

C. **Embryology**

The cloaca is a transient widening of the hindgut. It is divided during embryogenesis so that the digestive and urinary tracts of placental mammals exit the body separately. Abnormal cloaca development causes urogenital and anorectal malformations, which are among the most common forms of human birth defects. Despite extensive investigation, however, the process of mammalian cloacal morphogenesis remains a subject of controversy and speculation.

D. **Testing and Diagnosis**

In most instances, cloacal deformities can be diagnosed before birth with a prenatal ultrasound and may be confirmed by magnetic resonance imaging (MRI). At birth, the diagnosis may be confirmed or determined by physical examination with the hallmarks of relatively normal external female genitalia and a single opening in the perineum. A careful evaluation of structures of the upper urinary tract and sacrum is warranted, as well as perineal and pelvic anatomy, using a combination of ultrasonography, contrast injection with fluoroscopic imaging, and/or MRI.

E. **Initial Management of Cloacal Malformation**

Cloacal deformities require surgical repair. However, the immediate concern is to stabilize the newborn and identify and address any associated potentially life-threatening abnormalities. Initial surgical management involves the creation of a diverting colostomy to separate the rectum from the urinary and reproductive tracts in order to allow the passage of stool to the surface. With a colostomy, the large intestine is divided into two sections and the ends of the intestine are brought through surgically created openings (stomas) on the abdominal wall. The upper section allows stool to pass into a collection bag (appliance), while the lower section allows for drainage of mucus produced by the intestine (mucus

fistula).

Micturition difficulties are common. Urine often passes out of the bladder via a short urethra and then fills one or both (in setting of duplication) vagina(s). For those in whom help with evacuating urine is needed, a cystostomy or vaginostomy tube may be indicated. Vesicostomy may also be indicated in some children for longer-term bladder decompression. Some children will be able to void urine on their own, but for others, clean intermittent catheterization may be needed to help eliminate urine. The vagina must also be decompressed to allow the bladder, and at times the kidneys, to drain appropriately.

F. **Definitive Repair of Cloaca**

After stabilization and growth and/or correction of any significant associated anomalies, the anatomic features of the deformity will be clarified, and surgical correction planned. Definitive surgical treatment of cloaca typically involves the surgical creation of a urethra and advancement of vaginal structure(s) to the perineum. In some children with a less severe deformity, the urethra and vagina are well developed, maintained together, and they do not need to be created or separated. In these cases, the urethral and vaginal openings are advanced to the skin surface together as a single unit in a procedure called “urogenital mobilization.” Finally, a reconstruction of the bowel, through a procedure called a “pull-through” of the colon, must be completed. For this procedure, the surgeon may have to open the abdomen to complete the mobilization and advancement of the colon to the perineum. Ideally, for definitive repair of cloaca, advancement of the urethra, vagina, and anus to the surface are performed at the same surgical setting.

Dilation of the anus in order to prevent stenosis at the surface is necessary for several months following definitive repair. Once complete healing of the definitive cloacal repair has taken place, a third operation will be performed in order to close the colostomy and reestablish

normal bowel movements through the rectum. Additional urinary and/or reproductive tract surgery may be necessary.

G. **Outcomes**

The outcome for a child with a cloacal deformity depends on a number of factors, including the extent of the problem, associated anomalies, whether the sacrum is affected, and the technical exactness and healing of the operative procedure used to correct the problem. Serial bladder and bowel function evaluation is needed in all of these patients.

1. Mild deformity: More mild cases generally have a favorable long-term outlook. These children usually have excellent bladder control, normal sexual development and function (including fertility), and a near-normal pattern of bowel movements.
2. Severe deformity: Seventy to eighty percent of children will have a very favorable outlook with good to excellent stool control and only infrequent episodes of leakage or incontinence. The other 20% to 30%, depending on the degree of associated problems, will likely need a lifelong bowel and/or urinary bladder management program with a variety of medical and surgical interventions (as needed) to improve their quality of life.

V. PRUNE BELLY SYNDROME

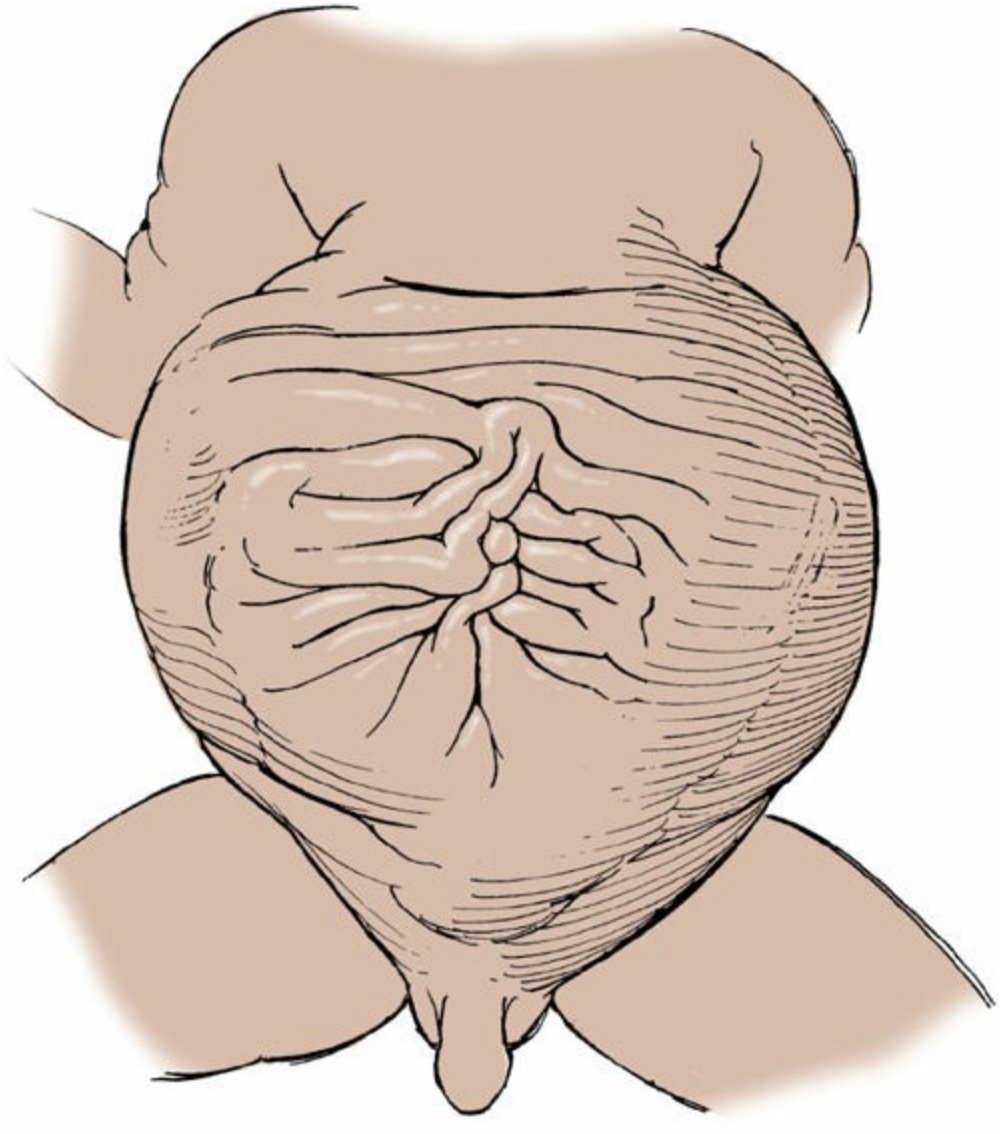


Fig. 16-5 Prune belly syndrome.

A. Background

Also referred to as Eagle-Barrett, triad, or mesenchymal dysplasia syndrome is characterized by three major pathologic anomalies: a deficiency or absence of abdominal wall musculature; a variety of ureteral, bladder, and urethral anomalies, manifested in most cases by marked dilation; and lastly, bilateral undescended testes (Fig. 16-5). Other coexisting orthopedic, pulmonary, and cardiac anomalies have been noted as well. The incidence ranges from 1 in 35,000 to 1 in

50,000 live births with most cases occurring in boys and 3% to 5% occurring in girls.

B. **Pathogenesis**

The etiology of prune belly syndrome (PBS) remains controversial, but two theories predominate.

1. Obstructive theory: This suggests that severe bladder outlet obstruction existed early in gestation and was subsequently relieved after irreversible damage had occurred. This obstruction resulted in bladder distention, ureteral dilation, and hydronephrosis as well as atrophy of the abdominal wall muscles by the increased pressure, mechanical distension, and interference with the blood supply of the organs involved. Most patients with PBS lack anatomic obstruction at the time of birth, however.
2. Mesodermal defect theory: A second theory suggests that because obstruction is rarely present at birth and there is a lack of bladder hypertrophy and hyperplasia, a primary defect in mesenchymal development occurs early in gestation.

C. **Clinical Manifestations**

1. Kidney: Renal abnormalities are the major determinants of survival, with a 20% chance of stillbirth or death in the neonatal period from renal dysplasia and the associated pulmonary hypoplasia. An additional 30% of patients will develop urosepsis or renal failure or both in the first 2 years of life.
2. Ureter: Severely dilated and tortuous, the ureters are most severely affected at the lower end and appear histologically to have patchy areas of fibrosis. Vesicoureteral reflux is present in 75% of these patients. Although their radiographic appearance is alarming, drainage is generally adequate.
3. Bladder: The bladder is generally capacious, smooth-walled, and irregularly thick, without trabeculation. Often a urachal remnant or diverticulum creates an hourglass configuration. Functionally, patients with

these bladders exhibit a diminished sensation of fullness, have a large capacity with poor contractility, decreased voiding pressures, and thus a poor ability to empty.

4. Prostate and posterior urethra: The prostatic urethra is elongated and characteristically tapers to the membranous region, which gives rise to the typical radiographic appearance of a triangular posterior urethra on voiding cystourethrogram.
5. Anterior urethra: Although the urethra is most often normal in this syndrome, both urethral atresia and megalourethra can be seen.
6. Testes: Cryptorchidism is seen universally in boys with PBS, the gonads characteristically being found high in the abdomen. Because they are intra-abdominal and may be injured further in bringing them down, and in addition, the prostate is underdeveloped and the bladder neck open, infertility is the rule. However, in recent years, pregnancies have been achieved using intracytoplasmic sperm injection after retrieval of the occasional sperm.
7. Abdominal musculature: The most characteristic manifestation of the syndrome is the wrinkled “prune-like” skin of the abdomen in the newborn infant. Skeletal muscle hypoplasia is seen in all three layers of the abdominal wall muscles. Complications are surprisingly minimal. The inability to sit up directly from the supine position may delay the onset of walking, but it rarely affects normal physical activity.
8. Associated anomalies: Other anomalies are found in over 65% of patients, the most common being cardiopulmonary and gastrointestinal, and including orthopedic and developmental problems as well. Pulmonary abnormalities range in severity, with the most significant arising in cases with associated antenatal oligohydramnios. Children who survive the

neonatal period usually have no associated pulmonary problems.

D. **Fetal Diagnosis and Treatment**

Antenatal ultrasound is capable of detecting abnormal urinary tract dilation as early as 14 weeks. However, it is difficult to differentiate PBS from other causes of urinary tract dilation. In the presence of oligohydramnios, prenatal intervention has been advocated to decompress the dilated bladder and restore the amniotic fluid volume. Although prenatal intervention may improve pulmonary function, improved renal function is uncertain. Furthermore, intervention in cases of PBS is difficult to justify because in utero obstruction may not exist.

E. **Management of the Neonate**

1. Immediate evaluation
    a. History and physical: Rule out life-threatening cardiac and pulmonary problems first. The abdominal examination is made much easier by the thin, relaxed belly, which permits easy palpation of the intra-abdominal and retroperitoneal contents.
    b. Serum creatinine: Creatinine levels in the first days of life reflect maternal values, but a progressive increase (or failure to decline) suggests some degree of renal insufficiency.
    c. Bladder stimulation test: Simple bladder massage can be used to stimulate a detrusor response, and one can use this as a test of voiding.
    d. Imaging
        (1) Ultrasound will provide important information on renal anatomy, degree of dilation of the urinary tract, and bladder emptying.
        (2) Voiding cystourethrography (VCUG) should be postponed to avoid introducing bacteria into a stagnant urinary tract.

Aggressive antibiotic treatment is essential around the time of any invasive study as the introduction of bacteria may result in UTI, pyelonephritis, and/or sepsis.

(3) A dimercaptosuccinic acid (DMSA) nuclear renal scan may be performed in order to evaluate for renal malformation/scarring.

2. Treatment: Management is based upon whether patients are *severely* affected (oligohydramnios, pulmonary hypoplasia, or pneumothorax), *moderately* affected with typical external features and uropathy of the full-blown syndrome but no immediate concern for survival, or lastly, have a *mild* form unlikely to develop urosepsis or azotemia. The third-category patients show internal features that may be mild or incomplete. Uropathy is less severe and renal function is stable.
    a. Severely affected: Patients in the severely affected category usually do not survive the neonatal period; however, for the few who do survive, urinary diversion by vesicostomy, cutaneous pyelostomy, or ureterostomy is often recommended to provide optimal urinary drainage.
    b. Moderately affected: The approach to moderately affected PBS patients is variable, but is usually nonoperative unless infection (despite antibiotic prophylaxis), failure of adequate renal growth, or decreasing renal function is encountered. In these cases the urinary tract is reconstructed with ureteral tailoring and correction of reflux to reduce stasis and infection risk. Reconstruction of the abdominal wall as well as orchidopexy are often performed simultaneously.
    c. Mildly affected: For mildly affected patients with good renal function, surgical intervention is

usually not necessary. However, life-long antimicrobial prophylaxis should be considered (in neonates, amoxicillin or first-generation cephalosporin; later, trimethoprim-sulfamethoxazole or nitrofurantoin). Orchidopexy may be delayed until such time as any other reconstructive procedures may become necessary or at about 6 months.

F. **Management into Childhood and Beyond**

Abnormalities of bladder function, in particular, in adequate bladder emptying, are the principal source of problems that may lead to renal deterioration.

1. Evaluation
    a. Urodynamics: The child with a low urinary flow rate and a significant residual volume should be evaluated with urodynamics.
2. Treatment
    a. In some cases, endoscopic evaluation of the urethra with internal urethrotomy of “pseudo-valves” may be necessary to reduce bladder outlet resistance although this remains controversial.
    b. Ureteral surgery: Although pyelonephritis or renal deterioration may prompt one to reimplant and perhaps tailor the ureters to improve drainage and prevent reflux, these procedures are complicated by the poor peristaltic nature of these ureters and the abnormal bladder into which they are reimplanted. Although the radiographic appearance of the urinary tract improves after surgery, it remains to be seen whether there is any long-term functional improvement. Because of persistent stasis postoperatively, nearly all these patients are maintained on lifelong antibacterial prophylaxis.
    c. Bladder function: Adequate drainage can be obtained with clean intermittent catheterization

(CIC), but this can be difficult as these patients have normal urethral sensation and some have urethral anomalies. For this reason, a continent abdominal stoma may be useful. If the family cannot catheterize the patient, a urinary diversion, usually a cutaneous ureterostomy, can be life-saving until the child is mature enough to perform the catheterization.

3. Prognosis
    a. Renal function: Patients who survive infancy with mildly impaired renal function may develop renal failure as a result of chronic pyelonephritis and reflux nephropathy. In these individuals, renal transplantation can be performed successfully. Many of these patients will need to perform CIC to alleviate chronic retention.
    b. Testicles: Early orchidopexy for intra-abdominal testes is warranted in boys with PBS because repair in infancy typically allows placement of the testes into the scrotum without division of the spermatic vessels. Although likely to be infertile, these patients may benefit from advances in assisted reproductive techniques.
    c. Abdominal wall: Reconstruction of the abdominal wall may be performed at the same time as orchidopexy. This procedure includes excision of redundant “prune-like” folds of skin, gathering of the underlying fascia and abdominal wall muscle, preservation of the umbilicus, and creating a satisfactory waistline. In milder cases observation may be the best option because of the tendency for the abnormal abdominal wall laxity to return over time.

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17 Adolescent Urology: Acute Scrotum, Varicoceles, and Delayed Puberty

Bruce J. Schlomer

I. ACUTE SCROTUM

Acute scrotum is defined by clinical presentation involving acute onset of scrotal pain and can include scrotal swelling, abnormal testis examination such as hardness or abnormal lie, or tenderness on examination of scrotal contents. The differential diagnosis for acute scrotum is quite broad. The most common diagnoses include torsion of the appendix testis, testicular torsion, and bacterial epididymitis (Table 17-1). The keys to correct diagnosis are clues in history, age of patient, physical examination, urine analysis findings, and scrotal ultrasound if needed.

TABLE 17-1 Distinguishing Testicular Torsion from Epididymitis

	Testicular Torsion	Epididymitis
Incidence	Accounts for 50–60% of acute scrotum cases in adolescents and 25% to 30% of cases in all pediatric patients.	Accounts for 20% of acute scrotum cases in adolescents, and less than 1% in prepubertal boys.

History	Acute onset of scrotal pain. The patient can usually state the exact time the pain began. Patients may or may not be sexually active. Urethral discharge usually not present. Usually not associated with voiding complaints. Nausea and vomiting are often present.	Gradual onset of pain. Patients are usually sexually active. Urethral discharge may be present: thin and watery suggests chlamydia; thick and purulent suggests gonorrhea. Dysuria may be present.
Physical Examination	Patients appear uncomfortable and in distress. High-riding testis. Absence of cremasteric reflex is usually found. Testis is hard and can be swollen. Overlying edema and scrotal redness suggests	Early: An enlarged and tender epididymis that is distinct from testis. Later: Entire testis and epididymis swollen and tender. No distinction between epididymis and testis. Most adolescents present later making it difficult to distinguish epididymitis from

	longer course of torsion.	testis torsion.
Laboratory	Urinalysis negative. Scrotal ultrasound with absence of blood flow to testis. Heterogeneous parenchyma suggests longer-standing torsion.	Urinalysis usually reveals numerous leukocytes. Nucleic acid amplification tests positive for gonorrhea or chlamydia. Scrotal ultrasound with hyperemia of epididymis and testis

A. **Torsion of Appendix Testis or Epididymis**

Torsion of the appendix testis or appendix epididymis typically presents in childhood before puberty and is the most common cause for acute scrotum in prepubertal males (Fig. 17-1). The pain can come on gradually but also can present rather acutely. On examination, the affected side typically has moderate to severe tenderness; inflammation or induration in epididymis can be appreciated along with tenderness localizing to epididymis; and the testis/epididymis can become very swollen and hard with overlying reddish change to the skin. The “blue dot” sign, which is not commonly seen, describes a dark-colored area or dot near the upper pole of the testis, which corresponds to the appendix testis or epididymis that has torsed.

Scrotal ultrasound typically shows increased vascular flow to the epididymis and occasionally an avascular area near the epididymis which is the torsed appendix. A urine analysis is normal. A diagnosis of “epididymitis” is often assigned based on ultrasound findings. While there is inflammation in the epididymis, this is not a bacterial

infection. Pain and induration typically improve over 2 to 4 weeks and treatment is supportive with ibuprofen, limiting activity, and ice packs if needed.

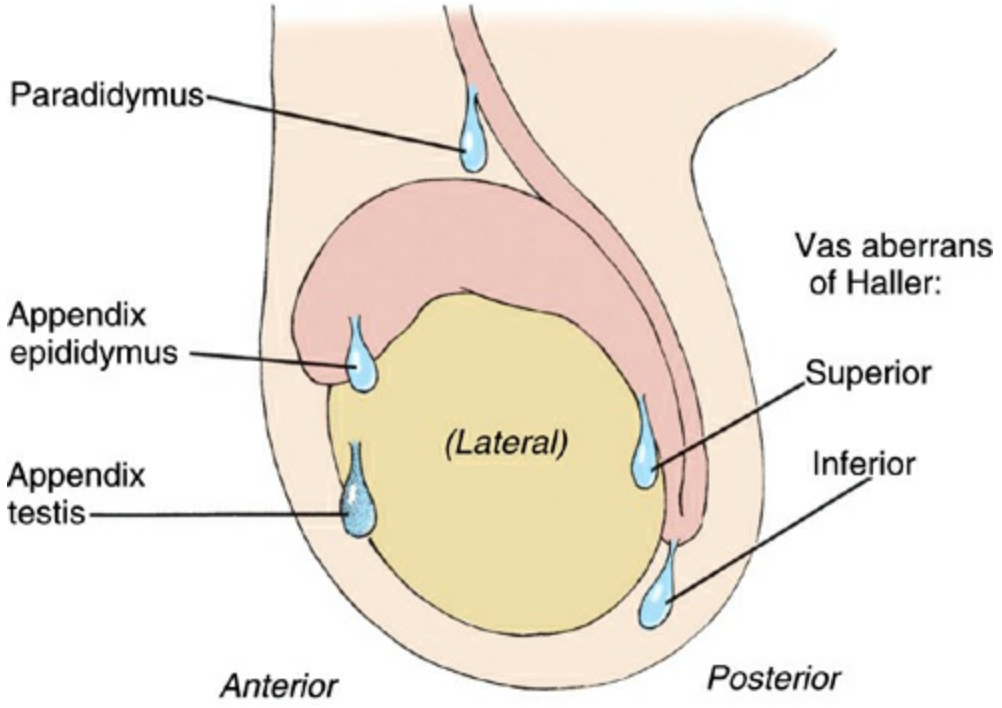

Fig. 17-1 Location of appendix testis and appendix epididymis.

B. Testicular Torsion

Testicular torsion most commonly presents in the neonatal period or peripubertal period. Neonatal testicular torsion typically presents at birth with a swollen, red, and hard scrotum. The pathology is extravaginal torsion of the spermatic cord. Management is somewhat controversial but options include immediate orchiectomy and contralateral orchiopexy, delayed contralateral orchiopexy, and observation. Asynchronous contralateral extravaginal torsion in the neonatal period is very rare, but the effects are devastating and this often drives families and urologists to proceed with immediate orchiectomy and contralateral orchiopexy.

The most common type of testicular torsion is intravaginal torsion. This type of testis torsion is the most common cause for acute scrotum in the peripubertal age

range. The pathology involves twisting of the spermatic cord inside the tunica vaginalis and resultant ischemia to the testis. A bell-clapper deformity predisposes to intravaginal testicular torsion and may be present bilaterally. Presenting symptoms and signs include acute scrotal pain, very tender testis, abnormal lie or high-riding testis, hard testis, absent cremasteric reflex, nausea/vomiting, and scrotal swelling.

The diagnosis of testicular torsion should be highly suspected in a peripubertal male with acute scrotal pain and some or all of the other findings. An ultrasound is usually obtained to confirm the diagnosis with high sensitivity and specificity. If the diagnosis is highly suspected, the patient should be taken to surgery without allowing any delay for an ultrasound. However, many centers can obtain an ultrasound very rapidly and confirm the diagnosis without significant delay.

The treatment for testis torsion in peripubertal period is emergent scrotal exploration, detorsion of testis, contralateral orchiopexy, and either ipsilateral orchiopexy or orchiectomy depending on viability of testis. Manual detorsion can be attempted to relieve ischemia but is not reliably successful. Rotating the testis laterally (opening a book) is initially recommended or under ultrasound guidance (Fig. 17-2). After around 6 hours of torsion, the risk for nonviability or subsequent testis atrophy increases significantly and after 24 hours, the risk for complete atrophy is 100% and orchiectomy is typically recommended. The decision to perform orchiectomy depends on how long the torsion has been present, intraoperative appearance of testis, and preoperative discussions with the family and patient. If the testis has a dark purple or black appearance that does not improve within 30 minutes of being detorsed, or there is no significant intraparenchymal blood flow on intraoperative Doppler ultrasound, or there is no significant intraparenchymal blood flow if the testis is incised, then

orchiectomy is recommended.

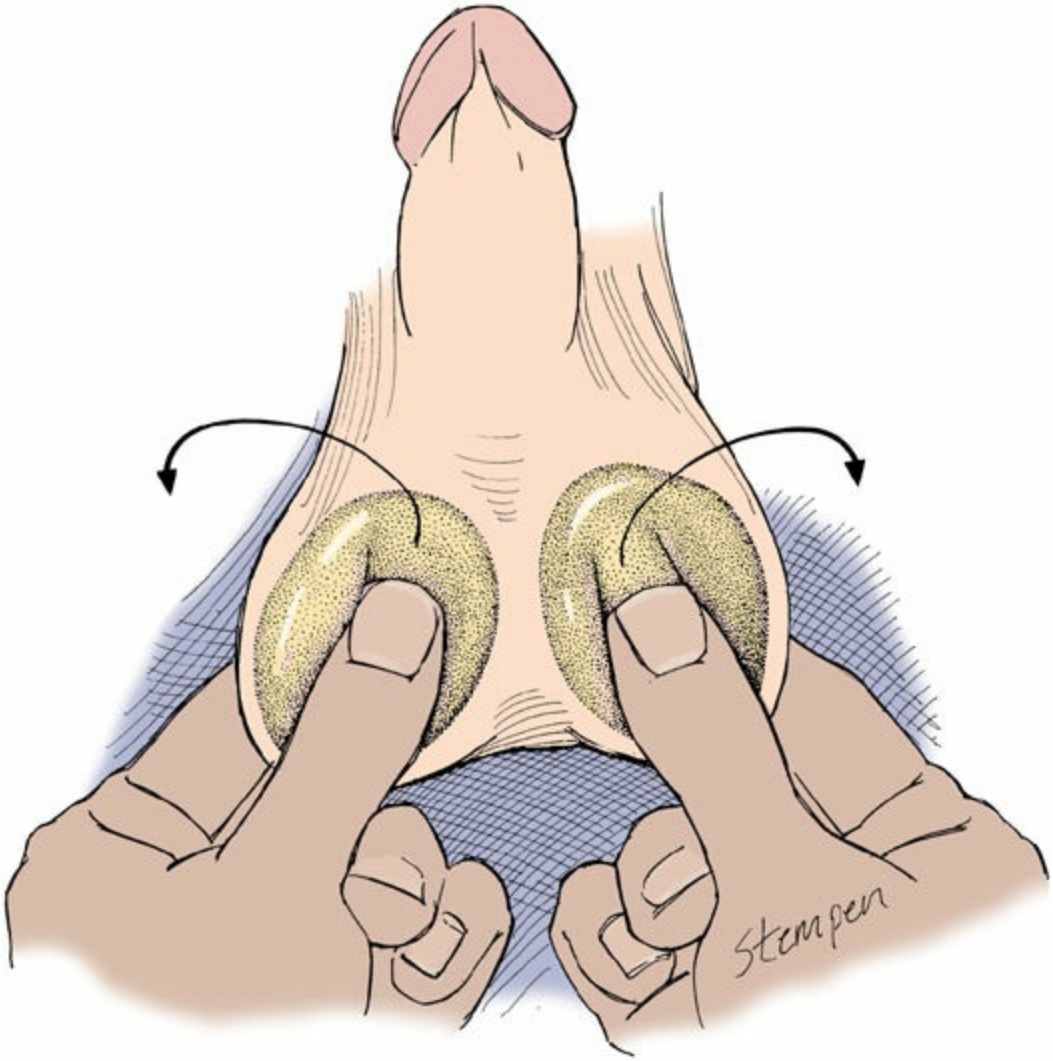

Fig. 17-2 Direction of rotation for manual detorsion of the testicle.

C. **Bacterial Epididymitis**

Epididymal inflammation from bacterial epididymitis is most common in postpubertal males who are sexually active, and is also seen in prepubertal males with congenital renal anomalies, or in patients who catheterize to empty bladder. The pain is generally more of a gradual onset but the amount of induration and swelling can range from mild and localized to the epididymis to quite severe involving the entire hemiscrotum. There may be fevers, dysuria, or other signs of sexually transmitted infections

(STIs) such as ulcers. The cremasteric reflex is generally intact and the pain is typically relieved by lying still. A history of UTIs or catheterization may be present. Abscesses can rarely form and can involve the epididymis or testis.

A urine analysis and urine culture should be obtained. A scrotal ultrasound typically shows hypervascular epididymis and testis. STIs such as chlamydia and gonorrhea should be tested for, as appropriate. In prepubertal males with bacterial epididymitis, a renal ultrasound and VCUG are recommended to evaluate for congenital anomalies such as ectopic ureter.

The treatment for bacterial epididymitis depends on the etiology. Broad-spectrum antibiotics are started for prepubertal males with bacterial epididymitis and UTI. Sexually transmitted diseases should be diagnosed and treated as needed. If gonorrhea is present, the patient should be treated for chlamydia as well. If any STI is diagnosed, the patient should be tested for additional STIs as appropriate and have the diagnosis reported to local public health department if required.

II. BENIGN CHILDHOOD URETHRORRHAGIA

Benign childhood urethrorrhagia is a condition that typically presents in males early in puberty. Patients complain of blood in their underwear (often noted by parents while doing the wash in an asymptomatic child), terminal drops of blood after voiding, and occasionally pain with urination. Urine analysis, urine culture, and renal ultrasound are normal. While this can be a concerning finding for patients and families, cases of benign childhood urethrorrhagia typically resolve over a matter of 12 to 24 months and no specific intervention is recommended. The etiology is thought to be due to early pubertal hormone exposure to the urethra leading to growth and friability of urethral mucosa that leads to bleeding and

pain with urethral distension during voiding. More frequent, smaller voids may help. For patients with long duration of symptoms, a VCUG and cystoscopy can be obtained but are also typically normal.

III. VARICOCELE

A varicocele is a dilation of the pampiniform plexus of spermatic veins above the testis (Fig. 17-3). Around 15% of postpubertal males will have a varicocele with 90% occurring on the left side only. The concern about varicoceles is their effect on future fertility in adulthood. While most men with varicoceles do not have infertility, there is a significant increased risk of infertility of around 20% with a varicocele compared to 5% in the general population.

Varicoceles can be explained by embryology and anatomy. The testes start near the kidneys in utero and then descend to the scrotum. This leads to the spermatic veins originating from the left renal vein and inferior vena cava on the right. These long spermatic veins have high pressure which may overcome valves and lead to dilated veins. Varicoceles are seen more frequently on the left because the left renal vein has a higher pressure than the inferior vena cava, and perhaps the left spermatic vein is more likely to have incompetent valves near the junction of the left renal vein.

Most varicoceles present after being found on physical examination by the pediatrician or by the patient. Occasionally they present with mild pain which is typically intermittent and dull in nature.

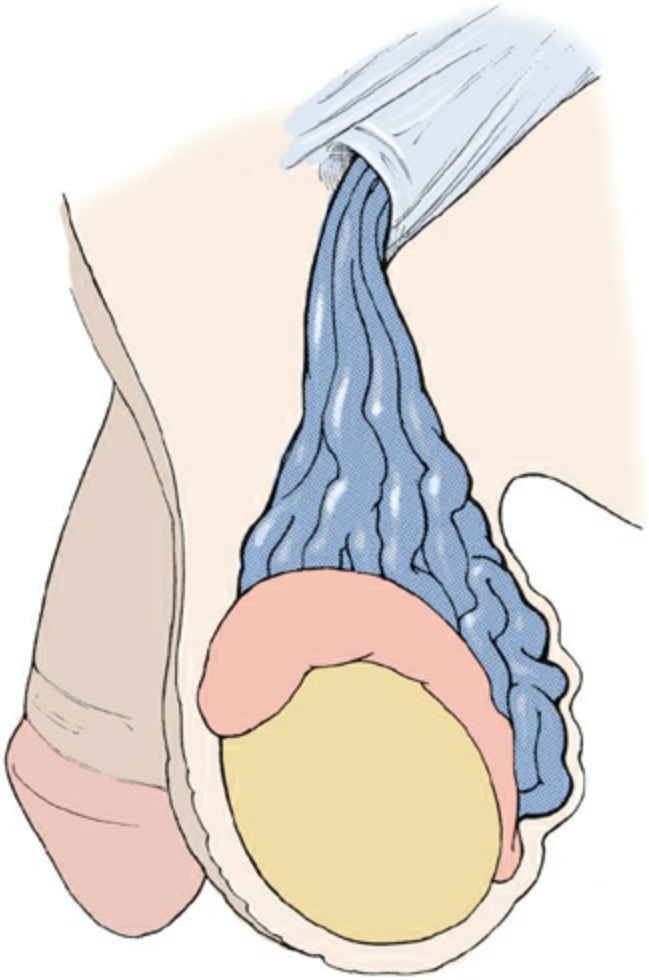

Fig. 17-3 Varicocele.

A. **Physical Examination**

A grade 1 varicocele can be palpated with Valsalva, a grade 2 can be palpated without Valsalva, and a grade 3 can be seen easily while the patient is standing. Most patients referred to pediatric urology clinics will have grade 3 varicoceles and have typical “bag of worms” appearance above the left testis. Other important findings to document on physical examination are Tanner stage, size of both testes, testes asymmetry, and total testicular volume. If the affected testis, typically the left, is smaller than the unaffected testis it is called testis hypotrophy.

B. **Radiology Evaluation**

Testis volume can also be measured with an orchidometer but a scrotal ultrasound is often obtained for this purpose

as well. While controversial, some centers report that scrotal ultrasound is more accurate in determining testes size.

If there is a grade 2 or 3 varicocele on the right side, especially unilateral, abdominal imaging should be obtained to rule out any intra-abdominal process such as a retroperitoneal tumor leading to obstruction of right spermatic vein.

C. **Indications for Surgery**

Commonly accepted indications for surgery in adolescents with a varicocele include pain or bother, affected testes 20% smaller than contralateral which does not improve over time, and low total testicular volume for Tanner stage. Some centers are more aggressive with surgery and will recommend surgery for lower levels of testis hypotrophy (10% to 15%) or recommend surgery when testis hypotrophy is detected without a waiting period to see if testis catches up on its own. In Tanner 5 males whose testes are fully grown, a semen analysis can be obtained that may help guide the decision for surgery or not. However, semen analyses are often difficult to obtain in this age group, especially in earlier Tanner stages.

D. **Observation**

Many or most patients will not have any indications for surgery or choose observation. In patients with testis hypotrophy, Q6 month physical examinations are reasonable. In patients without any testis hypotrophy, yearly physical examinations every 6 months are reasonable. Examinations should be continued until the end of puberty. If any significant testis hypotrophy does not improve, testis hypotrophy develops, or low total testicular volume develops, surgery should be discussed.

E. **Varicocelectomy**

The most common type of varicocele repair performed by pediatric urologists is a laparoscopic varicocele repair. Other types include inguinal approach, subinguinal

approach, and spermatic vein embolization. Important complications of varicocele repair include varicocele recurrence, hydrocele formation, and very rare testicular atrophy.

IV. DELAYED PUBERTY

A diagnosis of delayed puberty is defined by the absence of any secondary sexual characteristics at an age that is greater than the age that 95% of children of that sex and culture have started puberty. Patients with incomplete pubertal development can also be considered to have delayed puberty. The first sign of puberty in males is testicular enlargement and the first sign in females is breast development. The average age to start puberty in males is around 10 years with upper limit of normal 14 years. The average age to start puberty in females is around 10 years with upper limit of normal 12 years. The most common cause of delayed puberty is physiologic delayed puberty and typically patients are evaluated by endocrinologists for other causes of delayed puberty. However, there are several conditions that urologists should be aware of that may present with delayed or incomplete puberty.

A. **Klinefelter's Syndrome**
   Patients with Klinefelter's syndrome have 47 XXY karyotype and can present with delayed or incomplete puberty. They often have other characteristics typical of Klinefelter's syndrome such as tallness, small testes, azoospermia, gynecomastia, small phallus, and learning disabilities. Patients with Klinefelter's syndrome have high follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels during puberty and relatively low corresponding testosterone levels. Testosterone replacement is often needed for full virilization.
B. **Kallmann Syndrome**

Kallmann syndrome is characterized by delayed or incomplete puberty and lack or highly reduced sense of smell. The hypothalamus in these patients fails to produce adequate gonadotropin-releasing hormone (GnRH) which leads to hypogonadotropic hypogonadism. Kallmann syndrome is more common in males but can also occur in females. Several genetic mutations have been identified as causes. Treatment is hormone replacement. Fertility is possible but requires specialized treatment by a reproductive endocrinologist.

C. **Turner Syndrome**

Patients with Turner syndrome have an XO karyotype, female phenotype, and delayed puberty. They also have several other classic features such as webbed neck, low-set ears, short stature, low hairline on neck, broad chest with widely spaced nipples, palmar crease, and lymphedema of hands and feet in infancy. Several organ anomalies are associated with Turner syndrome including coarctation of the aorta, aortic valve anomalies, and horseshoe kidney. There is a wide spectrum of presentation and some females will present with only short stature and delayed puberty. Patients who are mosaic for Turner syndrome (45 XO, 46 XX) have fewer classic features and may have normal height. The diagnosis is confirmed by karyotype. These patients are typically infertile and management of growth hormone supplementation and estrogen supplementation by an endocrinologist is needed.

D. **Complete Gonadal Dysgenesis (Swyer Syndrome)**

Patients with complete gonadal dysgenesis or Swyer syndrome have a karyotype of XY but phenotypically appear female. Because the testes do not form and patients have nonfunctional streak gonads, there is no testosterone production and virilization in utero. In addition, since the gonads do not produce anti-müllerian hormone these patients have a uterus, fallopian tubes, and vagina. These patients usually present in adolescence with

lack of development of secondary sexual characteristics and amenorrhea. LH and FSH levels are elevated, pelvic ultrasound shows uterus present, and karyotype is XY. Treatment includes cyclic estrogen and progesterone replacement. Removal of the streak gonads are recommended due to significant risk of gonadoblastoma formation. Pregnancy is possible with use of donated eggs.

E. **Complete Androgen Insensitivity Syndrome**

Similar to complete androgen insensitivity, patients with complete androgen insensitivity syndrome (CAIS) have an XY karyotype but phenotypically appear female. The testes do form and secrete testosterone and anti-müllerian hormone. The androgen receptor does not sense testosterone, so virilization does not occur. The fallopian tubes, uterus, and upper vagina do not form because of the presence of anti-müllerian hormone. Patients with CAIS have normal or high levels of testosterone for pubertal males. Some of this testosterone is aromatized into estrogen which leads to breast development and feminization of body habitus. Pubic and axillary hair development is minimal along with acne development due to lack of androgen receptor. CAIS patients present with amenorrhea in adolescence or with inguinal hernias in childhood. The gonads are often removed at some point after puberty and estrogen replacement therapy is started, but timing of gonadectomy is somewhat controversial as the risk of tumors in the gonads is low. Vaginal length can be increased by dilations with some patients undergoing a vaginoplasty. CAIS patients are infertile.

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18 Genitourinary Trauma and Priapism

Hubert S. Swana and James M. Betts

I. INTRODUCTION

Trauma is the leading cause of morbidity and mortality in children. Five percent of all injured children sustain genitourinary trauma. Blunt traumatic injuries including falls, assault, sports injuries, sexual abuse, and motor vehicle accidents account for 80% of these injuries. Penetrating injuries such as falls on sharp objects, and knife and gun injuries constitute the remaining 20%. A significant number of children also have associated life-threatening injuries to the central nervous system, thoracic, and abdominal organs. Once the child has undergone initial stabilization and resuscitation, a careful and directed secondary survey can detect genitourinary injuries.

A. Renal Injury

The kidney is the most commonly injured genitourinary organ. Blunt trauma represents 80% to 90% of all renal injuries in children. Of all patients with abdominal trauma, blunt and penetrating, 8% to 12% sustain renal injury. The pediatric kidney is more susceptible to injury because of its large proportional size compared to the adult organ. The underdeveloped abdominal wall muscles and ribs, lack of perirenal fat, and its lower abdominal position do not provide as much protection for the pediatric kidney. In addition, congenital anomalies such as hydronephrosis, horseshoe kidney, and renal ectopia make a child's kidney more vulnerable to trauma.

1. Evaluation (Fig. 18-1)
    a. Blunt renal trauma: In adults with blunt renal trauma, gross hematuria, or microscopic hematuria (greater than 50 red blood cells per high-power field [RBCs/hpf]) with shock (systolic blood pressure lower than 90 mm Hg), are indications for genitourinary imaging. These criteria are inadequate for children. Up to two-thirds of children with grade 2 or higher renal injuries have a normal urinalysis. Children are also able to maintain normal blood pressures in the face of significant blood loss. Pediatric trauma patients with gross hematuria or microhematuria (greater than 50 RBCs/hpf) and hypotension should be evaluated for the presence of a renal injury. Additionally children who sustain injuries from rapid deceleration or high-velocity accidents, falls from over 10 feet, or direct flank injuries (baseball bat, helmet, or stick injuries) warrant study. Flank contusions, lower rib and vertebral fractures, and multisystem injuries after deceleration injuries can be accompanied by renal injury and require evaluation, even in the absence of hematuria.
    b. Penetrating renal trauma: Any child with hematuria and a penetrating injury to the flank, abdomen, or chest should be evaluated for the possibility of genitourinary injury.

       In stable children, contrast-enhanced computed tomography (CT) is the best choice. Intravenous (IV) pyelogram is reserved for intraoperative evaluations when CT scanning is not possible.

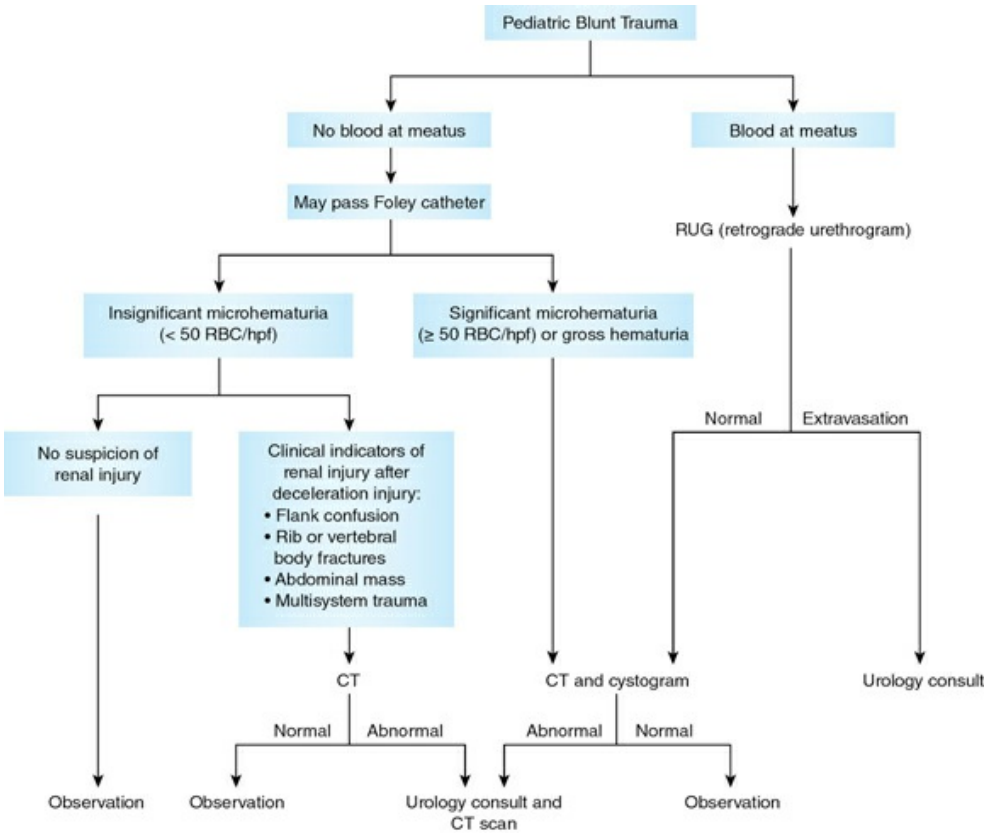


Fig. 18-1 Algorithm for the systematic radiographic evaluation of a child with suspected urinary tract injury after blunt trauma.

2. Imaging
   a. Ultrasonography: Many pediatric trauma centers utilize ultrasonography to rapidly screen trauma patients. Focused assessment with sonography for trauma (FAST) examination is highly specific (able to rule out significant injury). Specificity rates between 95% and 100% have been reported. The ability of FAST to detect significant injury (sensitivity) is variable and operator-dependent. Sensitivity rates vary widely from 22% to 96%. Due to these limitations, FAST examination is useful in specific situations. It can quickly rule out a hilar injury in an unstable patient. It can also be combined with serial physical examinations as part of observation protocols in selected stable patients.

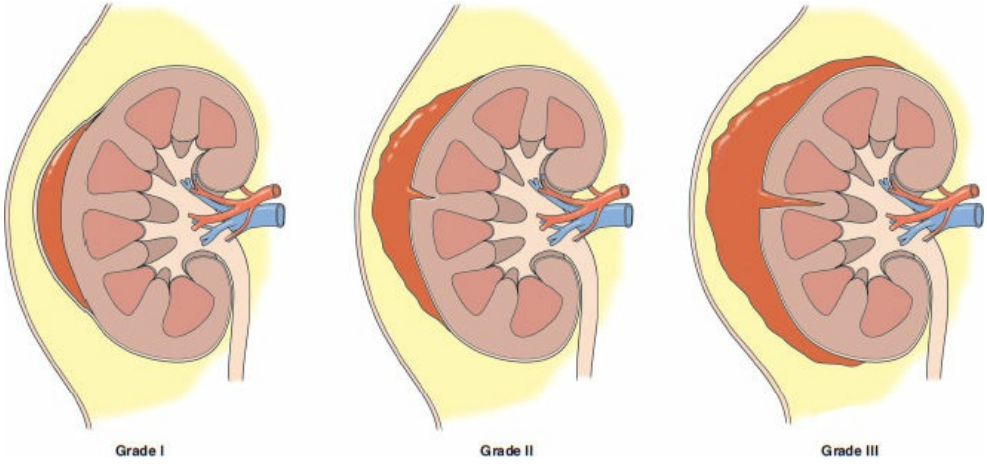
b. Computed tomography: A triphasic abdominal and pelvic CT study that combines a precontrast scan, a second scan 1 to 3 minutes after IV contrast, and a third delayed scan 10 minutes later, is the most sensitive and specific test available to detect urologic injuries. Many centers try to limit pediatric radiation exposure and perform a single-phase scan after injection of contrast. Single-phase CT scans, however, can miss urinary extravasation seen in renal and ureteral injuries.

CT scanning is essential for accurate staging of renal injury. In 2011, Buckley and McAninch revised the American Association for the Surgery of Trauma (AAST) renal injury grading system (Table 18-1, Fig. 18-2). No changes were made to grades 1 to 3. Grade 4 injuries now include all collecting system, renal pelvis, and segmental vessel injuries. Grade 5 injuries are now limited to injuries to the main renal artery and/or vein, including avulsion, laceration, and thrombosis. They are associated with higher exploration rates and lower rates of renal salvage.

TABLE 18-1 Renal Location Injury Definition

Grade 1	Parenchyma	Subcapsular hematoma and/or contusion
	Collecting system	No injury
Grade 2	Parenchyma	Laceration less than 1 cm in depth and into cortex, small hematoma contained within Gerota's fascia
	Collecting system	No injury

Grade 3	Parenchyma	Laceration greater than 1 cm in depth and into medulla, hematoma contained within Gerota's fascia
	Collecting system	No injury
Grade 4	Parenchyma	Laceration through the parenchyma into the collecting system, vascular segmental vein or artery injury
	Collecting system	Laceration, one or more into the collecting system with urinary extravasation
Grade 5	Parenchyma	Main renal artery or vein laceration or avulsion of the main renal artery or vein thrombosis



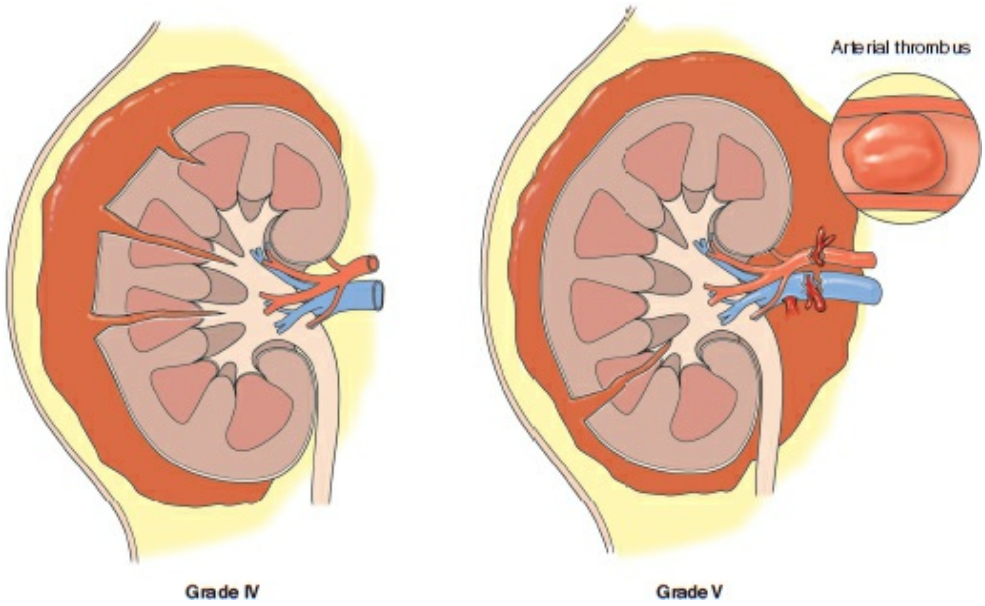


Fig. 18-2 Renal injury grading system (grades 1 to 5).

c. Intravenous pyelography (IVP): Occasionally trauma patients are taken to the operating room and require emergent exploration with possible nephrectomy. A single shot IVP (using 2 mL/kg of IV contrast followed by an X-ray 10 to 15 minutes later) can help identify the presence of a normal functioning contralateral kidney.

3. Management
   a. Nonoperative management: More than 90% of blunt renal injuries can be managed nonoperatively. Nonoperative management is recommended for low-grade (grades 1 and 2) renal trauma due to both blunt and penetrating injuries. Isolated high-grade injuries (grades 3 to 5) can also be managed nonoperatively if the patient is hemodynamically stable. Patients can be kept on bedrest until the urine clears. The patient's hematocrit is monitored to determine if bleeding has subsided. Prophylactic antibiotics are given in the case of urinary extravasation and the possibility of infected urine. Light activity is advised for 2 weeks to prevent delayed bleeding

and an imaging study is obtained at 3 months to assess function and rule out hydronephrosis. Repeat imaging is used for patients with persistent bleeding, prolonged ileus, and new or continued fevers. Up to 15% of patients with high-grade injuries (grades 3 to 5) managed nonoperatively require intervention for a symptomatic urinoma and 25% for persistent or delayed hemorrhage.

(1) Cystoscopy, ureteropyelography, and stent placement: Cystoscopy and retrograde ureteropyelography can helpdiagnose ureteropelvic junction (UPJ) injuries and can allow placement of double J stents for patients with symptomatic urinomas. Percutaneous nephrostomy tubes can help with urinoma management.

(2) Angiographic embolization: Angiography can help identify bleeding renal vessels. Selective embolization of renal branches helps avoid the need for open exploration 80% of the time. Embolization techniques are also useful in patients with persistent urinary fistulae and post-traumatic pseudoaneurysms.

b. Operative management: Certain situations mandate immediate exploration. Intervention may also be necessary in patients managed nonoperatively. The need for surgery depends on the child’s hemodynamic stability, the presence of additional injuries, and accurate radiologic assessment of renal injury.

(1) Renal exploration: Exploration is required in any patient with hemodynamic instability due to uncontrolled renal hemorrhage. Children with an expanding pulsatile retroperitoneal hematoma found during

laparotomy also require exploration. Exploration is recommended for patients with high-grade renal injury (grades 3 to 5), who undergo exploration for duodenal, colonic, and pancreatic injuries. Patients with disruption of the ureteropelvic junction require repair. Exploration is also required for patients with persistent bleeding after angiographic embolization. Some children undergo emergency laparotomy before CT scanning can be performed. If a renal hematoma is encountered, a 1-shot IVP can confirm contralateral renal function and renal exploration is recommended.

(2) Renal salvage: Attempted salvage by renorrhaphy and/or partial nephrectomy requires early vascular control, complete renal exposure, debridement of nonviable tissue, and control of bleeding vessels. Repair of collecting system injuries with placement of stents and nephrostomy tubes is performed as needed.

(3) Nephrectomy: This may be necessary in the hemodynamically unstable patient with multi-organ trauma and high-grade renal injury (grades 4 to 5). Patients with hypothermia and coagulopathy may not tolerate prolonged renal repair/salvage and may also require nephrectomy.

B. **Ureter**

Ureteral injuries are rare (less than 4% of all penetrating trauma) and most often due to gunshot or stab injuries. Ureteral injuries are accompanied by abdominal organ injury up to 90% of the time. Severe blunt injuries can cause tearing and disruption of the ureteropelvic junction (Fig. 18-3).

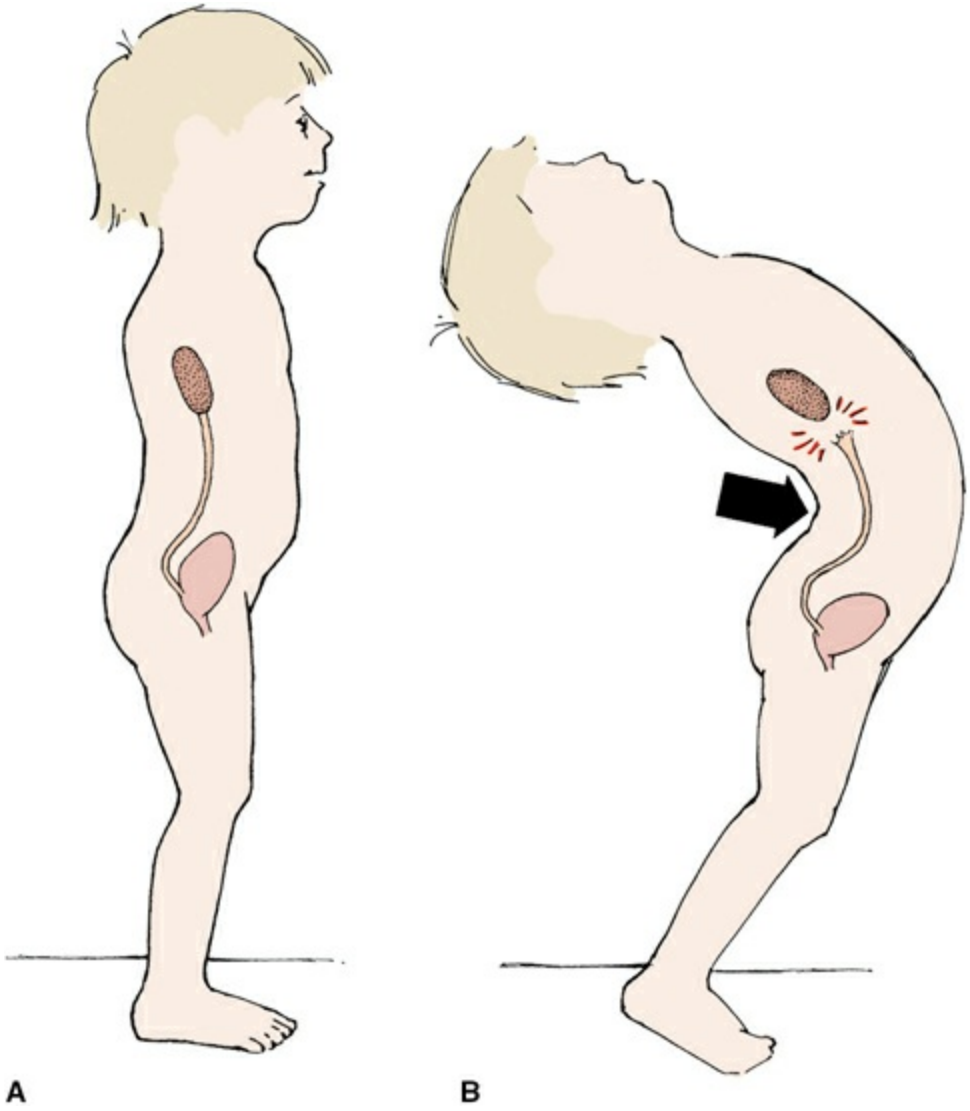


Fig. 18-3 A: Normal relation of the urinary tract to the spine in a child. B: With a sudden blow to the back, the ureter tenses against the hyperextended vertebral column and avulses at the ureteropelvic junction.

1. Evaluation: Ureteral injuries are frequently missed. One must maintain a high index of suspicion. Hematuria is present only 23% to 45% of the time. Historically, IVP and single-phase CT may miss up to 75% of cases. Direct visualization at the time of surgery and retrograde pyelography are more reliable. Delayed imaging studies should be obtained in patients with unexplained abdominal findings after penetrating flank and abdominal trauma. High-velocity (greater than 350 m/s) gunshot injuries can

cause necrosis of ureteral blast injuries. If drains have been placed, patients present with increased drain output 3 to 5 days after injury. They can also present with urinoma and/or infection of extravasated urine.

2. Management: In patients with UPJ disruption, repair is recommended within 5 days of injury if possible. If there is a delay in diagnosis of 6 days or more after injury, nephrostomy tube placement with delayed repair is recommended. Gunshot injuries to the ureter require adequate debridement of devitalized tissue, tension-free watertight repair along with internal stent placement and periureteral drainage.

C. **Bladder and Urethra**

The vast majority of bladder injuries occur after blunt abdominal trauma sustained in motor vehicle accidents. Around 89% of patients with bladder rupture have a pelvic fracture. Blood at the urethral meatus is a harbinger of urethral injury. Posterior urethral injuries are associated with pelvic fracture. Straddle injuries are a common cause of injury to the bulbar urethra.

1. Evaluation: If blood is found at the urethral meatus, retrograde urethrography (RUG) should be performed. The patient is placed in an oblique position. Elevation of one hip with a towel and 90-degree abduction of the downside leg is performed. A small catheter is advanced about 2 cm to 3 cm into the meatus. The balloon is filled with 1 cc of water to secure in place. Films are taken during injection of 20 cc of contrast material.

   If no meatal blood or urethral injury is identified, careful attempt at passing a well-lubricated catheter can be performed. If hematuria is discovered (greater than 5 RBCs/hpf), a cystogram is performed. Complete imaging includes a lower abdominal scout film, a film after bladder distention, and a post-drainage film. Pediatric bladder capacity can be estimated using the formula {(age in years + 2) × 30

cc} with a maximum of 300 cc.

2. Management: If one finds urethral extravasation, immediate urologic consultation should be obtained. Suprapubic cystotomy may be required. Urologic consultation is advised for bladder rupture as well. Intraperitoneal ruptures require immediate surgical repair. Uncomplicated extraperitoneal ruptures may be treated with catheter drainage alone. If a patient is undergoing exploratory laparotomy for other injuries or internal fixation of a pelvic fracture, extraperitoneal rupture repair is recommended.

D. **Scrotal and Penile Injury**

Scrotal and penile injuries usually occur with blunt injuries sustained in sports activities, straddle injuries, and bicycle falls. Scrotal hematomas can make assessment of testicular integrity difficult. Penile injuries can occur with blunt injuries such as from toilet seats. Tourniquet injuries from hair, rubber bands, or entrapment in zippers are not uncommon. Scrotal and penile lacerations can also be seen, and animal bites can occur rarely.

1. Evaluation: Scrotal ultrasonography is very helpful in evaluating testicular integrity. The tunica albuginea can be carefully studied. Testicular rupture usually appears as an intratesticular area of hypoechogenicity and discontinuity of the tunica albuginea.

   Evaluation of penile injuries should assess the underlying corpora and urethra (RUG) as well as the extent of skin defect. Penile fracture can occur after direct trauma to an erect penis but is extremely rare in prepubertal males.

2. Treatment: Scrotal hematomas with intact testicles can be managed with scrotal support, bedrest, and pain medications. Patients with testicular rupture should undergo emergent exploration and repair. Nonviable and extruded seminiferous tubules should be excised and closure of the tunica performed. The majority of patients managed emergently can avoid

orchiectomy. Patients with tense scrotal wall hematomas may require delayed drainage.

Penile and scrotal lacerations should be closed primarily with chromic catgut sutures after careful debridement and copious irrigation. If injury to the urethra or corpora is discovered, urologic consultation should be obtained. Antibiotic prophylaxis and tetanus and rabies immunizations are used as needed. In the majority of cases, good functional and cosmetic results are achieved.

E. **Vaginal Injuries**

Vaginal injuries may be associated with sexual abuse, foreign body insertion, or the same blunt pelvic forces that cause bladder and pelvic injuries.

1. Evaluation: If multiple injuries are suspected, stabilization is paramount. Circumstances surrounding the trauma and careful medical historical review are necessary if abuse is suspected.
2. Management: Vaginal laceration may require repair for hemostasis. Vaginoscopy, cystoscopy, and rectal examinations are necessary to ensure that bladder, vaginal, urethral, and anorectal injuries are not overlooked. If sexual abuse is suspected, a trained sexual-abuse examiner and authorities should be contacted immediately (see Chapter 29).

II. PRIAPISM

Priapism is a condition characterized by a prolonged painful erection in the absence of sexual desire. Treatment of priapism varies, depending on whether the patient has low-flow or high-flow priapism. Most priapism cases in children are the low-flow ischemic type (veno-occlusive). It must be considered a urologic emergency because prolonged and recurrent low-flow priapism is associated with corporal ischemia and can cause fibrosis and subsequent impotence. Prepubertal patients, if treated early, tend to have a better prognosis than adults.

A. **Etiology**

The most common cause of priapism in children is sickle cell disease. Up to 5% of boys with sickle cell disease have priapism. Priapism can occur as an isolated event or with other manifestations of sickle-cell crisis. Sludging of sickle cells impairs venous outflow. Leukemia is another important cause of priapism. Here abnormal (leukemic) cells impair penile venous drainage. For these reasons a complete blood count (CBC) must be obtained early in the evaluation of the priapism patient. High-flow priapism or nonischemic (arterial) priapism is usually associated with perineal or penile trauma.

B. **Diagnosis and Treatment**

Initial treatment is usually directed at the underlying cause. A detailed medical history combined with corporal venous sampling can usually differentiate between low- and high-flow priapism. In equivocal cases, penile and perineal color Doppler ultrasonography can be helpful. For sickle cell patients, one should increase the ratio of normal hemoglobin to hemoglobin S with transfusions or exchange pheresis. Additionally hydration, alkalinization, and analgesia should be used. When priapism persists despite these measures for more than 4 hours, intervention is necessary. Options include corporal aspiration, irrigation, and glans-cavernosal shunting.

High-flow priapism does not require emergency treatment. Cases of spontaneous resolution have been reported in children. Ice and compressive dressings are occasionally effective and should be used first. Selective arterial embolization is challenging in small children but is sometimes necessary. Surgical ligation of the internal pudendal or cavernosal arteries often leads to permanent erectile dysfunction.

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19 Hematuria

Kara N. Saperston

Hematuria in children is defined as greater than 5 red blood cells per high-power field (RBCs/hpf) in the urine on microscopic examination. Most children with hematuria have a benign condition that requires no intervention and that has an excellent prognosis. The incidence of significant disease is low (1% to 7%) with random screening. Since the finding of isolated microscopic hematuria is frequently transient, we recommend documentation on at least 2 of 3 consecutive urinalyses a few weeks apart before pursuing further workup. Hematuria may be microscopic (typically found in asymptomatic children discovered by routine dipstick screening of urine) or macroscopic, also called gross (apparent to the eye as a bright red or brownish discoloration of the urine). When positive, urine dipstick reagents change color and are indicative of the presence of RBCs (at least 5 RBCs/hpf), hemoglobin, or myoglobin. To distinguish among them, microscopic examination should be performed on a properly centrifuged, freshly obtained urine specimen (10 mL of urine spun at 3000 rpm for 5 minutes) to confirm the presence of RBCs, before the diagnosis of hematuria is made. Diagnostic studies should be reserved for those patients who by history, physical examination, and initial laboratory screening tests are deemed to be at high risk for serious renal or urologic disease. Greater than 40% of the time, children with gross hematuria have no identifiable cause. The most

common cause of non-glomerular gross hematuria is urinary tract infection (UTI), hypercalciuria, or stones. Around 15% to 20% of patients with painless micro- or macroscopic hematuria have hypercalciuria. Extensive and invasive random laboratory investigations in a child with isolated hematuria are unnecessary and discouraged. The most common cause of glomerular gross hematuria in children is acute postinfectious glomerulonephritis from streptococcal infection of the throat or skin. The presence of proteinuria may warrant diagnostic workup and coordination with a pediatric renal specialist. Causes of hematuria in children are listed in Table 19-1.

TABLE 19-1 Causes of Hematuria

A. Glomerular disease
- Benign familial hematuria/thin basement membrane disease
- Alport syndrome
- Acute post-infectious or chronic glomerulonephritis
- IgA nephropathy
- Membranoproliferative glomerulonephritis
- Systemic vasculitis: Henoch-Schönlein purpura, systemic lupus erythematosus, Wegener's granulomatosis, microscopic polyangitiis nodosa
- Hemolytic uremic syndrome

B. Non-glomerular disease
- Interstitial nephritis
- Infection: bacterial (UTI, tubercular), viral (BK, polyomavirus, HIV), parasitic (schistosomiasis, malarial)
- Acute tubular necrosis
- Polycystic kidney disease: autosomal dominant, autosomal recessive
- Tumor: Wilms tumor, angiomyolipoma, renal cell, transitional cell
- Obstructive: hydronephrosis

Hematologic: sickle cell anemia, renal papillary necrosis, hemophilia
Disseminated intravascular coagulopathy
Nephrocalcinosis, nephrolithiasis, hypercalciuria
Medications: NSAID, warfarin, heparin, cyclophosphamide, ifosfamide, hydralazine, thiouracil, allopurinol, penicillamine
Physiologic: exercise, fever, crush injury
Trauma
Vascular anomaly

C. Rare causes
Nutcracker syndrome: hematuria from trapping of the left renal vein between the superior mesenteric artery and the aorta
Sexual abuse/foreign body insertion
Loin pain/hematuria syndrome: diagnosis of exclusion

D. Newborns
Renal venous thrombosis
Renal artery thrombosis
Autosomal recessive polycystic kidney disease (ARPKD)
Urinary tract infection
Obstructive uropathy
Bleeding/clotting disorder

I. EVALUATION

A. History

In addition to determining the type, duration, and the pattern of the hematuria, a complete history of previous illnesses and associated genitourinary symptoms, medication use, and activity are essential in the workup of a child. One needs to differentiate between surgical and medical etiologies of the hematuria. There are a number of clues in the history that help to better define the etiology of the disease. Important historical and familial features, and the possible corresponding diseases are listed in Table 19-2.

TABLE 19-2 Historical Features and Associated Diseases

Patient history	Associated disease
Urinary frequency, dysuria, suprapubic, costovertebral or flank pain	Urinary tract infection, pyelonephritis, nephrolithiasis
Previous illness: respiratory illness, sore throat, or pyoderma	Postinfectious glomerulonephritis
Diarrhea	IgA nephropathy
Gross hematuria	Urinary tract infection Perineal irritation Trauma Nephrolithiasis IgA nephropathy Postinfectious glomerulonephritis Benign urethralgia Tumor Schistosomiasis
Medications (penicillin, nonsteroidal anti-inflammatory drugs, protease inhibitors)	Interstitial nephritis
Joint involvement, cough, hemoptysis, microscopic polyangiitis nodosa trauma	Systemic lupus erythematosus, Wegener's granulomatosis, kidney contusion
Edema, oliguria, proteinuria, hypertension	Glomerular disease
Failure to thrive, short stature, polyuria	Tubular disorders
Family history	
Microscopic hematuria	Benign familial hematuria

	Alport syndrome Hypercalciuria Nephrolithiasis
Hearing loss	Alport syndrome
Renal disease (insufficiency, dialysis, or transplantation)	Alport syndrome Polycystic kidney disease
Urolithiasis	Hypercalciuria
Sickle cell disease	Sickle cell nephropathy

B. **Physical Examination**

1. Blood pressure should be measured in all children regardless of age, using an appropriately sized cuff.
2. Growth parameters should be plotted on standardized growth charts.
3. Assessment of patient's skin for rash, petechiae, purpura, pallor, or edema should be done.
4. Abdominal examination should evaluate for palpable masses, signs of trauma, and localization of pain or tenderness.
5. Assessment of external genitalia for signs of inflammation, trauma, or the presence of a foreign body should be carried out.

Distinguishing features on examination and the corresponding diseases are listed in Table 19-3.

TABLE 19-3 Physical Findings and Associated Diseases

Physical Examination	Associated Disease
Hypertension	Chronic renal insufficiency Polycystic kidney disease Reflux nephropathy
Failure to thrive	Chronic renal insufficiency
Rash (petechiae, purpura, malar)	Henoch-Schönlein purpura Systemic lupus erythematosus
Edema	Proteinuria/nephrotic

	syndrome Fluid retention/acute renal failure
Abdominal mass	Polycystic kidney disease Hydronephrosis Tumor
Costovertebral or suprapubic pain	Urinary tract infection Pyelonephritis
Pallor	Hemolytic uremic syndrome Chronic glomerulonephritis Chronic renal insufficiency

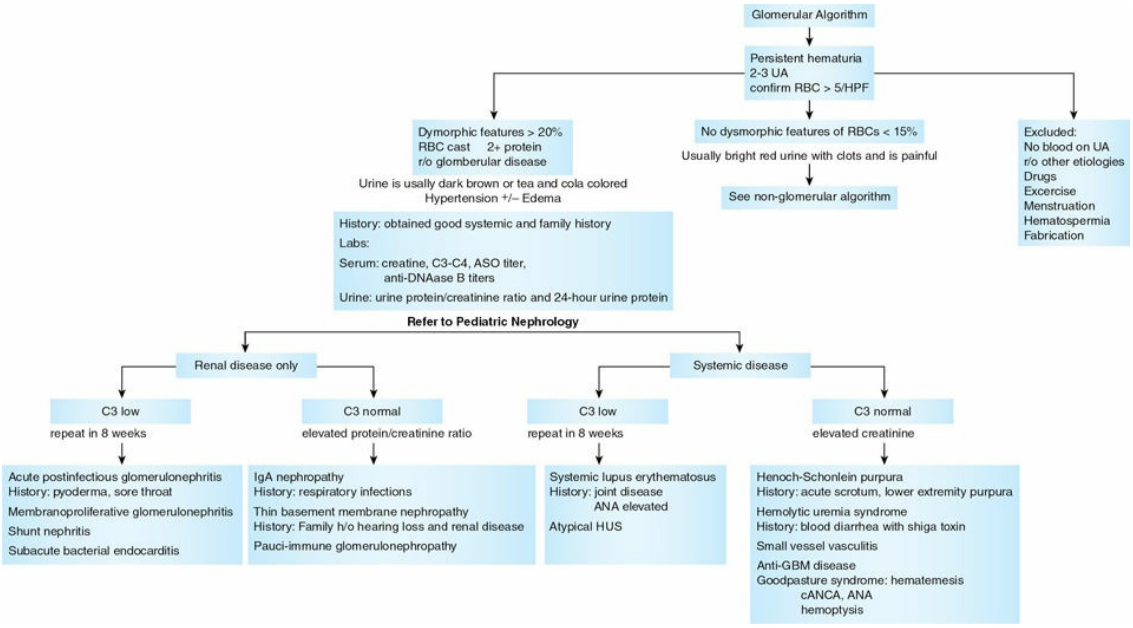
C. **Laboratory Investigation**

Once the diagnosis of hematuria is confirmed on at least two separate occasions over a 2- to 3-week period, a complete urinalysis should be obtained in each patient. Macroscopic or gross hematuria is classically associated with hematuria of glomerular origin. Color is important to evaluate. A red color without RBCs that is heme positive is due to myoglobinuria or hemoglobinuria. It takes one 1 ml of blood/liter of urine to induce a visible color change. Some medications like phenazopyridine and beetroot can also turn the urine red. In cases of brownish, “tea-colored,” or “Coca-Cola colored” hematuria glomerular disease can be considered, which is also supported by the additional findings of proteinuria, hypertension, edema, or azotemia. In contrast, macroscopic hematuria of extrarenal origin is bright red and frequently associated with pain and blood clots.

The examination of urinary RBC morphology by microscopy can be helpful in determining the site of origin, that is, glomerular versus non-glomerular. As RBCs pass through small disruptions in the glomerular capillary wall due to glomerular disease, RBCs become dysmorphic with distorted and irregular contours, and this is consistent with glomerular disease. Although phase

contrast microscopy is the traditional method for examining RBC morphology in urine specimens, many clinicians can evaluate the morphology on routine microscopy. RBCs with normal morphology represent hematuria from trauma, cystitis, and lower urinary tract malignancies. The finding of urinary RBC casts is diagnostic of glomerular disease and is not seen with extrarenal bleeding. Mild proteinuria from the release of hemoglobin from RBCs may be found in all types of hematuria.

For those children with gross hematuria or persistent hematuria (urine dipstick with heme 1+ or greater on two separate occasions over a 2- to 3-week period) that warrant further diagnostic evaluation, an algorithm for laboratory tests is provided in Figure 19-1.



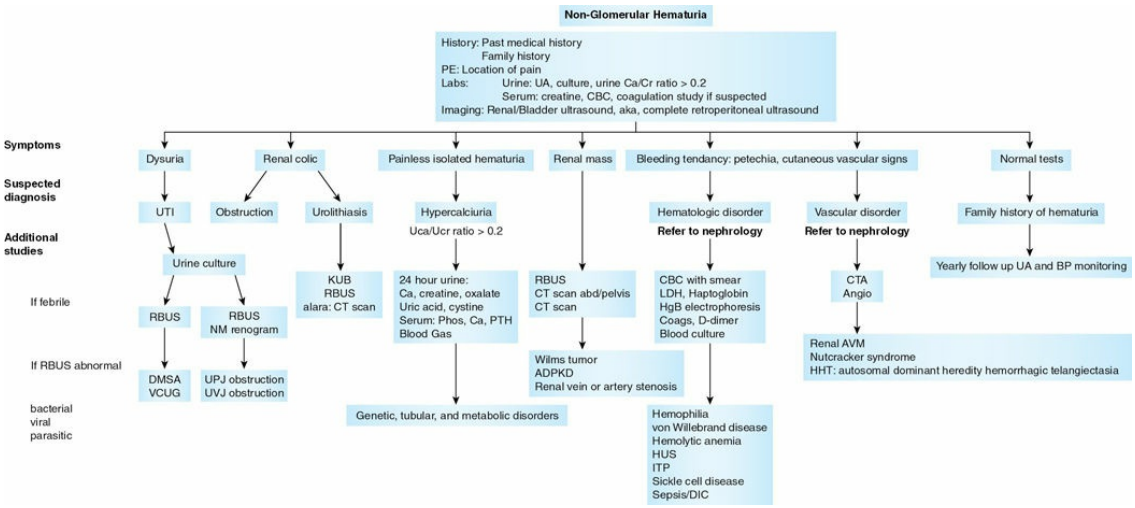


Fig. 19-1 Treatment algorithm for the child with hematuria. *UA*, urinalysis; *RBC*, red blood cell; *HPF*, high power field; *r/o*, rule out; *h/o*, history of; *ASO*, antistreptolysin O; *ANA*, antinuclear antibody; *HUS*, hemolytic uremic syndrome; *GBM*, glomerular basement membrane; *ANCA*, anti-neutrophil cytoplasmic antibodies; *PE*, physical examination; *UTI*, urinary tract infection.

The remainder of the urinalysis provides information that may be helpful in determining the cause of persistent hematuria (Table 19-4). Of importance are the findings of leukocytes (infection, interstitial nephritis), bacteria (infection), WBC casts (pyelonephritis), RBC casts (acute glomerulonephritis, other glomerular diseases), proteinuria (quantity: nephrotic vs. non-nephrotic amount), and dysmorphic RBCs (renal vs. non-renal origin). If the urine dipstick or microscopic evaluation reveals evidence for an infection, a urine culture is warranted.

TABLE 19-4 Additional Laboratory Evaluation

Laboratory Screen	Further Diagnostic Tests
Urine dipstick	
Nitrite and esterase positive	Urine culture
Proteinuria (normal C_3)	Serum albumin, hepatitis B surface antigen, cholesterol, 24-hour collection for protein, renal

	ultrasound; consider renal biopsy
Urine microscopic examination	
WBCs, bacteria, WBC casts	Urine culture
Dysmorphic RBCs, RBC casts	Serum creatinine, CBC, C_3, ASO and anti-DNase B titers
Urine calcium/creatinine ratio ≥ 0.2–0.3	24-hour collection for calcium, serum bicarbonate, urine pH, renal ultrasound
Persistent low C_3 (greater than 8 weeks)	ASO and anti-DNase B titers, ANA

If glomerulonephritis is suspected, measurements of serum creatinine, complement component 3 (C_3), complete blood count (CBC), antistreptolysin O (ASO), and anti-deoxyribonuclease B (anti-DNase B) titers should be determined. Other screening tests should also include both the measurement of the ratio of the urine calcium to urine creatinine and the checking of other family members for the presence of hematuria. Patients with persistent hematuria and proteinuria, significant proteinuria (spot protein to creatinine ratio greater than 0.5 to 1 in the urine) or nephrotic syndrome, elevated serum creatinine, hypertension, or low C_3 levels 8 to 10 weeks from presentation should be referred to a pediatric nephrologist for further evaluation and potential renal biopsy. Indications for renal biopsy are age of onset less than 1 year, gross hematuria with hypertension, abnormal renal function and associatedsystemic features, persistently low C_3 levels beyond 8 weeks, positive family history of renal failure, and hearing loss.

If the initial screening tests are normal in a patient with persistent asymptomatic microscopic hematuria, no further diagnostic evaluation is necessary and the patient should have an annual urinalysis and blood pressure

measurement.

II. ETIOLOGY OF HEMATURIA

The more common diseases causing hematuria in children are discussed briefly below. For each individual patient, a differential diagnosis can be made based on the knowledge of the likely etiologies and their characteristic features.

A. Glomerular Basement Disorders

1. Benign familial hematuria (thin basement membrane disease): In children and young adults, this condition manifests as persistent microscopic hematuria in the absence or presence of mild proteinuria. This condition differs from Alport syndrome as follows.
    a. Deafness and ocular abnormalities are not seen.
    b. Deterioration of renal function is rare.
    c. Thickening and splitting of the glomerular basement membrane

    are not seen in renal biopsy specimens examined by electron microscopy (although renal biopsy is only rarely indicated in these patients).

    In a patient with persistent microscopic hematuria, the diagnosis of benign familial hematuria should be strongly considered when either the screening of family members by urine dipstick is positive for blood or the family history reveals microscopic hematuria without deafness or progressive renal insufficiency. No particular mode of inheritance has been elucidated in this disease even though it is known to cluster in families. This diagnosis is usually made on clinical grounds; however, definitive diagnosis requires examination of renal tissue for electron microscopy obtained by biopsy (peripheral glomerular capillary basement membrane shows decreased thickness

of 265 nM or less). Despite the persistence of microscopic hematuria for many years, this condition is benign and nonprogressive, and therefore requires no therapy.

2. Alport syndrome: Alport syndrome (hereditary nephritis) is characterized by renal disease that initially includes hematuria and proteinuria, and later, progressive renal insufficiency. Alport syndrome is caused by a mutation in the type IV collagen gene that leads to an abnormal basement membrane. Other involvement includes sensorineural deafness and ocular abnormalities. Males are more severely affected than females. Since there are no specific laboratory findings in this disease, the definitive diagnosis requires a renal biopsy. In most cases, however, Alport syndrome can be diagnosed clinically in a child with microscopic hematuria in whom a positive family history of either Alport syndrome or sensorineural deafness with progressive renal insufficiency is obtained. Such children should undergo audiologic evaluation.

   Since there is no known therapy that alters the progressive course of Alport syndrome, the management of these patients requires close attention to those abnormalities associated with renal insufficiency. For those patients whose disease progresses to end-stage renal failure, renal replacement therapy includes dialysis or kidney transplantation.

B. **Glomerulonephritis**

Glomerulonephritis is defined histologically as inflammation of the glomeruli and can be acute, subacute, or chronic. Clinical features of acute glomerulonephritis include both macroscopic and microscopic hematuria, including the presence of red blood cell casts, proteinuria, edema, oliguria, hypertension, and increased serum levels of both urea nitrogen and creatinine (azotemia). Although

the classic form of glomerulonephritis, acute post-streptococcal glomerulonephritis (APSGN), often presents as a serious illness with many of these features, glomerulonephritis may also be detected incidentally by the findings of microscopic hematuria or proteinuria on a routine urinalysis.

The glomerulonephritides have been classified histologically with the different types defined by characteristic patterns observed on renal biopsy. These types can exist as primary renal diseases or as renal manifestations of systemic diseases. The causes of most forms of glomerulonephritis, whether intrinsic to the kidney or as part of a systemic disease, are unknown, but their pathogenesis often involves immune-mediated mechanisms, such as the glomerular deposition of antigen–antibody complexes. Although the prognosis of most of the glomerulonephritides is better in children than in adults, chronic glomerulonephritis is nevertheless one of the commonest causes of end-stage renal disease in older children and adolescents. The two most common forms of glomerulonephritis in children, acute post-streptococcal glomerulonephritis and immunoglobulin A (IgA) nephropathy, are discussed below. For those cases of glomerulonephritis with significant renal involvement, see Chapters 22 and 23 for the management of acute or chronic renal failure.

1. Acute post-streptococcal glomerulonephritis (APSGN): After throat or skin infections with certain strains of group A streptococci, glomerulonephritis may develop after a latent period of 1 to 3 weeks. APSGN is primarily a disease of children, with a peak incidence at age 7 years; it is rare in infants. Males are affected twice as commonly as females. The disease can present in both sporadic and epidemic forms. The pathogenesis is incompletely understood but appears to involve the deposition of a streptococcal antigen in the glomeruli with

subsequent inflammatory reaction. APSGN is a diffuse proliferative glomerulonephritis and is the classic example of this pathologic form, although the same pathology also can be observed in glomerulonephritis that follows other bacterial and viral infections. There is marked variability in the clinical presentation and course of the disease, although the majority of patients present acutely with hematuria (more often tea-colored gross, rather than microscopic), hypertension, oliguria with edema, and azotemia. The signs and symptoms of nephritis usually subside within 1 to 2 weeks, although microscopic hematuria and, especially, low-grade proteinuria may persist for months or even years. Complete recovery occurs in more than 95% of children.

In addition to nonspecific laboratory findings that include mild anemia and increased serum levels of creatinine and urea nitrogen, the diagnosis of APSGN depends on the demonstration of elevated serum titers of antibodies against streptococcal antigens (pharyngitis: ASO; impetigo: anti-DNase B titers) and decreased serum complement (C_3) levels. Serum C_3 levels return to normal within 8 to 12 weeks of onset; however, antibody titers to streptococcal antigens remain elevated for 4 to 6 months. If the C_3 level remains persistently low after 8 to 12 weeks from onset, this would suggest the glomerulonephritis associated with systemic lupus erythematosus or membranoproliferative glomerulonephritis. Since the majority of patients with APSGN recover completely, a renal biopsy is not necessary. However, a renal biopsy should be considered when the C_3 level remains low for longer than 8 to 12 weeks or if there is persistent azotemia, significant proteinuria, and/or hypertension.

Most patients receive symptomatic treatment for

fluid retention, which includes salt and fluid restriction, and for hypertension, the use of diuretics such as furosemide, and antihypertensive drugs such as hydralazine and nifedipine. If a streptococcal infection is still present, antibiotics are indicated but they do not shorten the duration of the nephritis.

2. IgA nephropathy: IgA nephropathy is the most common cause of glomerulonephritis and is primarily a disease of children and young adults and is rare in infants. Males are affected twice as frequently as females. The etiology and pathogenesis are unknown. The typical presentation features intermittent and recurrent episodes of macroscopic hematuria, or the finding of microscopic hematuria with or without proteinuria on routine urinalysis. The former usually occurs during or shortly after an upper respiratory tract infection and spontaneously resolves after several days. In most children with IgA nephropathy, blood pressure and renal function are normal at the time of diagnosis. However, a small percentage of affected children can present with acute glomerulonephritis or nephrotic syndrome and are at risk of progression to complete renal failure after the onset of disease.

   Although the definitive diagnosis by renal biopsy reveals deposition of IgA in glomeruli on immunofluorescence, the pattern of gross hematuria occurring in association with upper respiratory infection is so characteristic of IgA nephropathy that a presumptive diagnosis can be made without a renal biopsy. However, this pattern also occurs in children with hereditary nephritis (Alport syndrome), Henoch-Schönlein nephritis, and rarely in benign familial hematuria. Patients who present with gross hematuria characteristic of IgA nephropathy and nephrotic-range proteinuria (greater than 3.5 grams or 50 mg per kg per 24 hours), azotemia, or hypertension are at

risk for a poorer outcome and may require a renal biopsy for prognosis and guidance in therapy. Unfortunately, there are no controlled studies demonstrating a beneficial effect of treatment on either the acute or long-term course of patients with IgA nephropathy. Nonetheless, corticosteroids in patients with poor prognostic features are often used. Patients with IgA nephropathy require close, long-term follow-up.

3. Membranoproliferative glomerulonephritis (MPGN): Membranoproliferative glomerulonephritis (MPGN) is one of the less common causes of glomerulonephritides and it affects both children and young adults. Renal involvement is variable in this disease and includes asymptomatic microscopic hematuria, proteinuria, nephrotic syndrome, and acute chronic glomerulonephritis. Diagnosis of MPGN is made by renal biopsy and further classified into subtypes (types 1, 2, and 3) by histologic, immunofluorescence, and electron microscopy findings. Renal biopsy is typically performed in any patient with persistent renal involvement and a blood C_3 level that remains low for more than 8 weeks. The pathogenesis of this disease is unknown. However, there is a significant proportion of cases with MPGN type 1 associated with hepatitis C infection. Although there is some suggestion that children may respond to alternate day corticosteroids, the majority of cases fail to respond to any therapy. In most children, the renal disease is usually chronic and there is progression to renal failure.
4. Systemic vasculitis
    a. Henoch-Schönlein purpura: It is a multisystem vasculitis that is seen commonly in children but rarely in adults. It typically involves the skin (palpable purpura most commonly affecting the extensor surfaces of the lower limbs), kidney

(hematuria, proteinuria, or glomerulonephritis), musculoskeletal system (joint pain or swelling), and gastrointestinal tract (vomiting or abdominal pain). The testes may also be affected. This disease is often preceded by an intercurrent illness. Since both the renal manifestations and the renal biopsy findings are similar to those found in IgA nephropathy (see above), the diagnosis is often made on clinical evidence of extrarenal involvement. Therapy is supportive and in severe cases, corticosteroids may be an effective treatment, similar to IgA nephropathy.

b. Systemic lupus erythematosus (SLE): Renal involvement in SLE can present with asymptomatic microscopic hematuria, proteinuria, nephrotic syndrome, or acute glomerulonephritis. Although SLE is most common in adult women, it can present in adolescence. If SLE is suspected by history (rash, joint complaints, etc.), physical examination, and laboratory tests (persistent low C_3 level), then additional blood tests should include an antinuclear antibody (ANA) test and an anti-double stranded DNA (anti-dsDNA) antibody test. A patient with SLE and an abnormal urinalysis, including isolated microscopic hematuria, warrants a renal biopsy. The histologic classification on renal biopsy, in addition to clinical symptomatology and laboratory findings, is used as a guide in determining the treatment (corticosteroids, cyclophosphamide, mycophenolate mofetil) for SLE.

c. Wegener's granulomatosis/microscopic polyangiitis nodosa: These disorders are caused by small vessel vasculitides and account for a large percentage of rapidly progressive

glomerulonephritis found in children. Similar to postinfectious glomerulonephritis, these disorders can present with microscopic hematuria, proteinuria, nephrotic syndrome, or acute glomerulonephritis. Extrarenal involvement in Wegener's granulomatosis usually involves upper respiratory tract (sinusitis) and lower respiratory tract (cough with pulmonary hemorrhage often associated with granulomatous lesions) and arthralgias. In contrast, microscopic polyangitiis nodosa involves the skin (palpable purpura), neurologic (mononeuritis multiplex), arthralgias; in some cases, lower respiratory tract (pulmonary hemorrhage) can be involved. Renal biopsy often shows focal or diffuse proliferative glomerulonephritis with extensive crescent formation. Serologically, these disorders are linked with the presence of antineutrophil cytoplasmic antibodies (ANCA). In Wegener's granulomatosis, the antibody staining is directed against the neutrophil cytoplasm (termed C-ANCA) with antigen specificity for proteinase 3 on enzyme-linked immunosorbent assay (ELISA). For microscopic polyangitiis nodosa, the antibody staining is perinuclear (termed P-ANCA) with antigen specificity for myeloperoxidase. For severe disease, treatment involves corticosteroids, cyclophosphamide, and in some cases, plasmapheresis.

C. **Urinary Tract Infection**

See Chapter 6.

D. **Hypercalciuria or Nephrolithiasis**

Hypercalciuria is defined as urinary calcium excretion greater than 4 mg/kg/day. Idiopathic hypercalciuria can result from either excessive gastrointestinal absorption of dietary calcium or from a renal leak of calcium due to

decreased tubular reabsorption. The hematuria associated with hypercalciuria is painless and can be either microscopic or macroscopic; the bleeding is thought to result from mechanical trauma to renal cells caused by calcium crystals. Typically, red blood cell casts and proteinuria are absent. On the other hand, nephrolithiasis is rare in children and its presentation is quite varied. Similar to hypercalciuria, the patient may have asymptomatic microscopic hematuria but more often presents with renal colic, abdominal pain, or gross hematuria. The child's medical history may provide significant clues to an underlying condition that predisposes stone formation.

To screen for hypercalciuria, a random urine sample is obtained for the calculation of the ratio of urine calcium concentration to that of urine creatinine concentration. A ratio of greater than 0.2 to 0.5 (age dependent) in a fasting morning specimen suggests excessive urinary calcium excretion. To confirm the positive screening test, a more accurate assessment is a 24-hour urine collection that should be obtained in an age-appropriate patient to determine the calcium excretion rate. A calcium excretion of greater than 4 mg/kg/day is considered abnormal. Additional tests to rule out other causes of hypercalciuria should include the serum level of calcium, phosphorus, vitamin D, and parathyroid hormone. A medication history is important to look for the administration of diuretics (furosemide). For example, furosemide therapy in infants with bronchopulmonary dysplasia can cause long-term hypercalciuria and lead to significant rickets of the long bones. A renal ultrasound should be performed at baseline to determine whether nephrocalcinosis or medullary sponge kidney is present. If nephrocalcinosis is found, a serum bicarbonate level and serum pH should also be measured to rule out renal tubular acidosis. Renal ultrasound can detect most stones not visualized on plain radiography; however, if the sonogram is nondiagnostic,

noncontrast CT scan of the abdomen can be definitive.

In isolated hypercalciuria, therapy is generally conservative and includes dietary salt restriction, which by decreasing urinary sodium excretion decreases calcium excretion. Intake of large volumes of oral fluid is recommended since this will dilute urinary calcium and avoid supersaturation, a condition necessary for stone formation. In particular, water and fresh lemonade (to increase urinary citrate levels, since citrate is an inhibitor of stone formation) are the best fluids. Hypercalciuric children with nephrocalcinosis or a history of passage of renal stones may require thiazide diuretics if limitation of sodium does not result in resolution of the hypercalciuria. Thiazide diuretics increase calcium reabsorption in the distal tubule resulting in reduced calcium excretion by the kidney. Large ureteral stones that do not pass require further evaluation by pediatric urologists with experience in endosurgical or lithotripsy intervention.

E. **Other Causes**

A history of strenuous exercise, blunt trauma to the abdomen, or a bleeding disorder should be apparent as potential etiologies of isolated hematuria. The occurrence of macroscopic hematuria following minimal trauma to the kidney should raise the possibility of hydronephrosis or a cystic kidney. African-Americans or any patient at risk for carrying the sickle cell trait should be tested for the presence of hemoglobin S. Heterozygotes as well as homozygotes for hemoglobin S can develop hematuria due to decreased medullary blood flow as a result of hypoxia and hypertonicity that induces sickling of RBCs within the renal medulla. This results in dilated capillaries in the pelvic mucosa, which can become congested and rupture, the presumed origin of the hematuria.

Isolated hematuria, or in rare instances, associated with proteinuria and reduced renal function, can be caused by interstitial nephritis secondary to medications. Medications that are associated with this condition

include nonsteroidal anti-inflammatory agents, protease inhibitors, penicillin, cephalosporins, phenytoin, cimetidine, furosemide, and thiazide diuretics. A history of recent or current use of one of these medications in a patient with hematuria should strongly support this diagnosis. In the majority of patients, withdrawal of the medication results in resolution of the urinary abnormalities.

RECOMMENDED READING

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20 Nephrolithiasis in Children: Medical Management

Gregory E. Tasian

I. INTRODUCTION

Nephrolithiasis (kidney stone disease) is a disorder of mineral metabolism characterized by acute painful presentations that recur for many patients. Nephrolithiasis has been associated with extrarenal diseases including cardiovascular disease, hypertension, diabetes, low bone-mineral density, and chronic kidney disease. Contrary to historic literature, most kidney stones that occur during childhood are not due to rare, inherited monogenic disorders such as cystinuria. As in adults, calcium-based stones are the most common type of kidney stones that develop during childhood. Currently, the prevalence of kidney stones is approximately 9%, which represents a 70% increase since the 1990s. Recent studies have shown the incidence of stone disease has increased substantially among children, with the greatest increases observed among adolescent females. The cause of the shift in the epidemiology of kidney disease over a short time period is unclear. The risk of nephrolithiasis is determined by the interaction of genetics, behaviors, and environmental exposures. This chapter will review the presentation, causes, evaluation, and medical treatment of urolithiasis in children.

II. PATHOPHYSIOLOGY

A. The following factors are known to affect the formation of kidney stones.

1. Hypercalciuria
2. Hypocitraturia
3. Hyperuricosuria (uncommon in children)
4. Hyperoxaluria
5. Low urine volume
6. Acid urine pH (uric acid stones, which are rare in children)
7. Alkaline urine pH (calcium phosphate stones).

Hypercalciuria is most commonly idiopathic. It is exacerbated by high dietary intake of salt and protein. Hypocitraturia may be idiopathic or related to metabolic acidosis, as in chronic kidney disease, chronic diarrheal states, and high protein diet. Hyperuricosuria is typically due to dietary purine excess and very rarely to genetic mutation.

B. **Comorbid Disease**

Other medical conditions increase the risk of nephrolithiasis by affecting urine chemistries, volume, and/or pH.

1. Metabolic disorders
    a. Hypercalciuric states
        (1) Idiopathic hypercalciuria
        (2) Primary hyperparathyroidism
        (3) Renal tubular acidosis
        (4) Corticosteroid excess
        (5) Immobilization
        (6) Medullary sponge kidney
        (7) Phosphorus depletion
        (8) Vitamin D intoxication
        (9) Idiopathic hypercalcemia of infancy
        (10) Malignancy
        (11) Bartter syndrome
        (12) Furosemide use in infants
        (13) Sarcoidosis

b. Hyperoxaluria
    (1) Primary hyperoxaluria (types I, II, and III)
    (2) Enteric hyperoxaluria from inflammatory bowel disease (e.g., Crohn's disease) and malabsorption (intestinal bypass)
c. Cystinuria
d. Hyperuricosuria
    (1) Leukemia, lymphoma
    (2) Idiopathic, familial
    (3) Inborn error of metabolism: hypoxanthine-guanine phosphoribosyltransferase deficiency (Lesch–Nyhan syndrome)
    (4) Glycogen storage disease, type I
e. Hypocitraturia
    (1) Renal tubular acidosis
    (2) Medullary sponge kidney
    (3) Malabsorption syndromes
f. Xanthinuria
g. Orotic aciduria

2. Abnormalities of the urinary tract
    a. Ureteropelvic junction obstruction
    b. Vesicoureteral reflux
    c. Neurogenic bladder
    d. Hydronephrosis
    e. Ileal conduit, ureterosigmoidostomy
    f. Bladder exstrophy.

III. INITIAL MANIFESTATIONS

Similar to adults, children with nephrolithiasis often present with the following symptoms.

A. Pain
B. Nausea/vomiting
C. Hematuria
D. Incidental stone on diagnostic imaging.

The frequency of these findings varies with age. Classic flank pain may not be seen in children, particularly those under 5

years of age.

IV. Stone Composition

Contemporary analyses of the mineral composition of kidney stones in children demonstrate that approximately 85% are calcium-based. The approximate proportion of stone types classified by the main component are as follows.

A. Calcium oxalate 75% to 80%
B. Calcium phosphate 10% to 15%
C. Magnesium ammonium phosphate (struvite) 5% to 10%
D. Cystine 1%
E. Other 1%.

The historic incidence of struvite stones is approximately two-fold higher in young children 0 to 5 years of age, than in adolescent patients. This reflects a higher association of urinary tract infection with stones in infants than in older children.

V. EVALUATION OF THE CHILD WITH UROLITHIASIS

A. Ultrasound should be used as the initial imaging study for children with suspected nephrolithiasis reserving CT only for children with a nondiagnostic ultrasound in whom the clinical suspicion for stones remains high. Although ultrasound is less sensitive and less specific than CT, ultrasound accurately identifies most clinically significant kidney stones in children. The diagnostic criteria for identifying a kidney stone are: (1) echogenic focus on greyscale image; (2) posterior acoustic shadow (often not seen on modern ultrasound machines); and (3) “twinkle” artifact on Doppler.
B. Following diagnosis and acute treatment of the symptomatic stone, initial evaluation should seek to identify underlying metabolic abnormalities because up to

70% of children with nephrolithiasis will have abnormalities in the urine that increase the risk of stone formation and may be targets for dietary and pharmacologic interventions. Hypercalciuria and hypocitraturia, both of which increase the risk of recurrent kidney stones, are the most commonly identified metabolic abnormalities.

C. Children with stones should undergo the following evaluation.
   1. Family history: The following historical features are important: personal and family history of kidney stone disease including type of stone, recurrent urinary tract infection, infection with urease-producing organisms (proteus), comorbid disease (particularly conditions noted in Section II, 2).
   2. Medications: Diuretic use, steroids, calcitriol, topiramate, zonisamide, acetazolamide, ketogenic or Atkins diet, supplemental vitamin C and D, and supplemental calcium.
   3. Physical examination, including blood pressure, height, weight.
   4. Biochemical evaluation of blood and urine.
      a. 24-hour urine (calcium, oxalate, citrate, uric acid, sodium, creatinine levels, volume, pH, cystine, and supersaturation profiles of calcium oxalate and calcium phosphate). For children and young adolescents, these values should be indexed to weight, body surface area, or creatinine level in order to be properly interpreted. Additionally, 24-hour creatinine excretion should be quantified to determine the adequacy of the collection. See Table 20-1.

TABLE 20-1 Normal Urinary Solute Excretion

Metabolite	Age	Random (mg/mg)	24-hour (use indexed values

			until patient has adult body weight)
Calcium	0–6 mo	<0.8	<4 mg/kg
	7–12 mo	<0.6	
	>24 mo	<0.21	
Oxalate	0–6 mo	<0.26	<40 mg/1.73 m^2
	7–24 mo	<0.11	
	2–5 y	<0.08	
	5–14 y	<0.06	
	>16 y	<0.03	
Citrate	0–17 y	>0.2–0.42	Males: >130 mg/g Females: >300 mg/g
	>18 y		Males: >450 mg/g Females: >550 mg/g
Cystine	>6 mo	<0.075	<50 mg/1.73 m^2
Uric acid	>2 y	0.56 mg/dL GFR (glomerular filtration rate)	<815 mg/1.73 m^2

b. Serum studies (basic metabolic panel, calcium, magnesium, phosphate, and uric acid).

5. Stone analysis: Chemical analysis of urinary stones should be performed whenever stone material is available for analysis. Depending on the composition

of the stone, subsequent metabolic evaluation of the patient should proceed accordingly.

VI. MANAGEMENT OF UROLITHIASIS IN CHILDREN

A. Management of the Symptomatic Stone

1. Pain: Treatment includes nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and narcotics.
2. Infection: After obtaining urine for culture, antibiotics should be administered to patients for whom urinary tract infection is suspected. The combination of infection and an obstructing stone requires emergency placement of a ureteral stent or nephrostomy tube.
3. Medical expulsive therapy (MET): Tamsulosin has been associated with increased passage of ureteral stones in children. For children younger than 4 years, doxazosin can be dosed more easily than tamsulosin. The mechanism for MET is dilation of the ureter due to high densities of $\alpha 1^{A}$, α_{1D}, and calcium channel receptors in smooth muscle of the distal third of the ureter and ureterovesical junction.
4. Urine should be strained to collect the stone should it pass spontaneously.
5. Indications for surgical intervention
    a. Obstructive stone in an immunocompromised patient
    b. Intractable pain despite adequate oral analgesia
    c. Inability to tolerate adequate oral intake
    d. Fever and suspected pyelonephritis
    e. Stone in solitary kidney
    f. Failure of spontaneous passage
    g. Repeated ED visits due to stone-related symptoms despite adequate oral pain control
    h. Parental/patient desire after counseling for nonobstructive stones.

6. Surgical management: Between 25% and 50% of children with nephrolithiasis are estimated to undergo surgical intervention. Current commonly used surgical options for nephrolithiasis include shockwave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PCNL) (see Chapter 21).

B. **Long-Term Management of Kidney Stone Disease**

1. Dietary modification
    a. Increase fluid intake to maintain a urine output of at least 30 mL/kg/day up to the adult goal of 2.5 L/day.
    b. Decrease sodium to less than 2 to 3 mEq/kg/day for young children or less than 2.4 g for adolescents with hypercalciuria or calcium-based stones.
    c. Decreasing oxalate intake may offer some benefit for patients with calcium oxalate stones.
    d. Regardless of stone risk, children should consume 100% of the recommended daily allowance of protein.
    e. Maintain normal dietary calcium intake.
2. Pharmacoprevention: The goal of therapy is to prevent kidney stone recurrence, which has been shown to be as high as 50% within 3 years of the index stone event. Specific therapy should be guided by knowledge of the underlying factors that predispose to stone formation in the individual patient.
    a. Thiazide diuretics (e.g., hydrochlorothiazide, chlorthalidone) are the first-line drugs for children with calcium stones and hypercalciuria. Thiazides are used after maximizing urine calcium reduction by limiting dietary sodium intake.
    b. Citrate therapy (usually potassium citrate) inhibits calcium stone formation by complexing

with calcium, thus decreasing the supersaturation of calcium in urine, and also by directly inhibiting crystal growth and aggregation. Citrate also alkalinizes the urine, which increases solubility of calcium oxalate, cystine, and uric acid.

c. Surveillance imaging: Guidelines for surveilling for new stone formation and stone growth have not been established for children. At the author's institution, renal bladder ultrasounds are obtained every 6 months for the first 2 years following the index stone and yearly for 5 years if the patient remains stone-free.

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21 Urolithiasis in Children: Surgical Management

Hubert S. Swana

I. INTRODUCTION

In the United States the incidence of nephrolithiasis in children is increasing. Studies from several different regions of the United States have demonstrated an increase in the number of clinic and emergency room visits along with hospitalizations due to nephrolithiasis. The incidence is higher in warm climates and in areas with immigrants from countries with endemic stone disease. Boys and girls appear to be equally affected. Currently 75% to 80% of pediatric patients have upper tract stones. Metabolic disorders are responsible for 50% of stones in children. Up to 22% of children with nephrolithiasis will require surgical intervention within 6 months of presentation. Of these patients, 25% will require more than one procedure.

Multiple factors must be considered when planning pediatric stone surgery. Patient age and size often require special instruments. Stone size and location may limit access to the stone. Stone composition is also important. Knowledge of anatomic abnormalities such as calyceal diverticula, ureteroceles, or ureteropelvic junction obstruction is important as well. Prior urologic surgery such as ureteral reimplantation may limit surgical options. Shock wave lithotripsy and ureteroscopy are used for smaller renal and ureteral stones

with similar stone-free rates. Larger renal stones require percutaneous nephrolithotomy, alone or in combination with shock wave lithotripsy or ureteroscopy. Open or laparoscopic surgery is rarely necessary.

II. SURGICAL MANAGEMENT

The initial management of children presenting acutely with symptoms of stone disease is no different than that of adults. Children should receive ample pain medications, antiemetics, and hydration as needed. Infection should be treated with antibiotics and when present, concomitant obstruction should be relieved quickly with either ureteral stent placement or percutaneous nephrostomy. Off-label use of alpha-1 blockers as medical expulsive therapy may be beneficial in children with ureteral stones. In all cases, renal imaging guides treatment (Fig. 21-1). In afebrile children with a stone less than 4 mm in size and no associated anatomic abnormalities, observation is appropriate. Failure of an observed stone to pass, uncontrolled pain, or intractable nausea and vomiting, even in the presence of a relatively small stone, are indications for intervention.

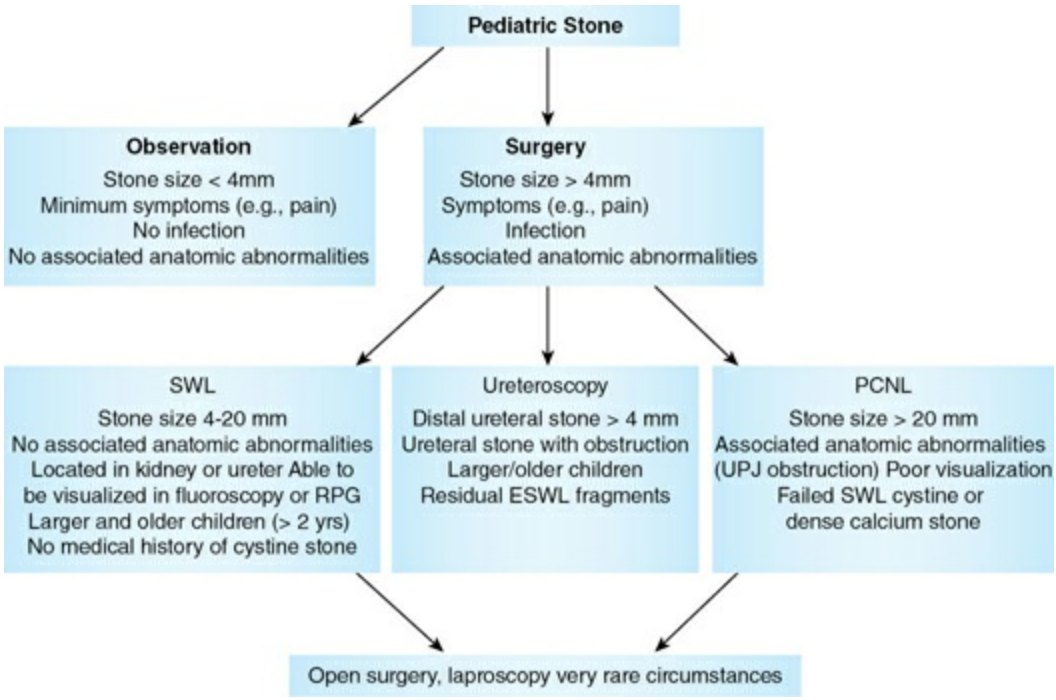

Fig. 21-1 Algorithm for management options for pediatric nephrolithiasis. *ESWL*, extracorporeal shockwave lithotripsy; *RPG*, retrograde pyelogram; *PCNL*, percutaneous nephrolithotomy

A. Shock Wave Lithotripsy

Shock wave lithotripsy is a noninvasive method of stone fragmentation (Fig. 21-2). Children have decreased shock wave attenuation because of their small size, which limits trauma to surrounding organs. Long-term studies indicate that after extracorporeal shock wave lithotripsy (SWL) children do not develop renal scarring. Renal function and linear growth do not appear to be affected and no increased risk of hypertension or other medical renal disease have been documented.

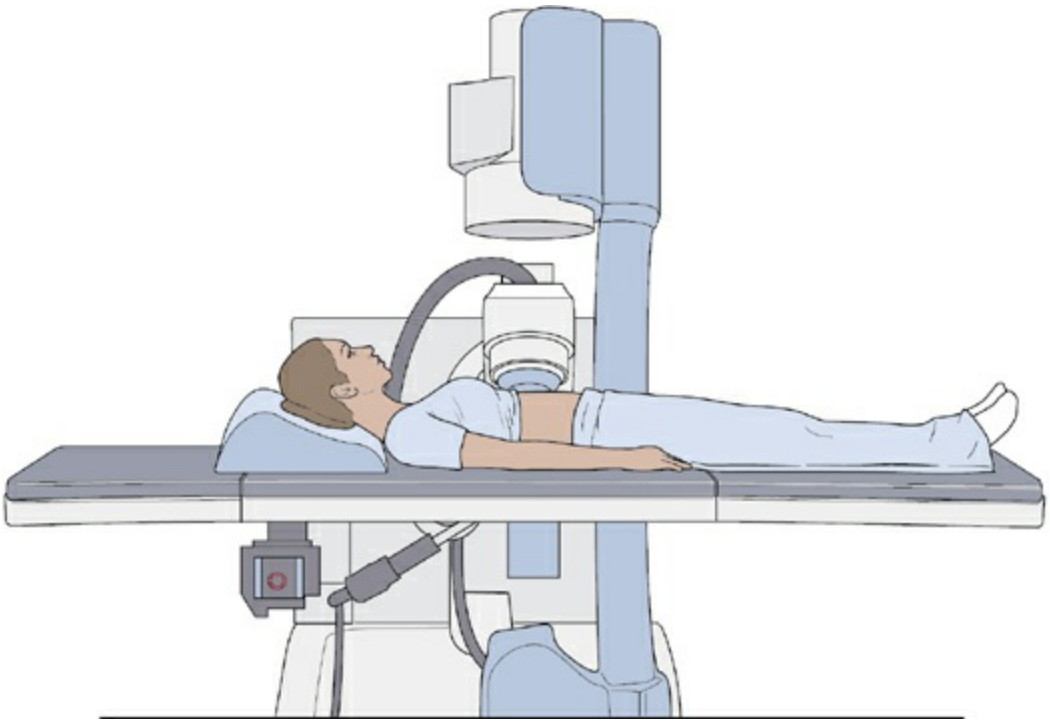

Fig. 21-2 Patient undergoing SWL calculi treatment.

In children with small to moderate upper tract calculi and no anatomic defect, SWL is an acceptable first-line therapy. Success with stones up to 1.5 cm in size has been reported. Most centers report a stone-free rate between 70% and 86% for medium-sized stones. Use of SWL in staghorn calculi is possible with reports of stone-free rates in excess of 70%; a significant number of these patients required one or more re-treatments. Older machines require fluoroscopy for stone localization. Reported complications include the accumulation of obstructing stone fragments in the distal ureter (steinstrasse), hematuria, flank pain, and urosepsis. In addition, the type of lithotripsy machine affects results greatly with newer machines, which are generally less powerful, having lower stone-free rates.

B. **Ureteroscopy**

Small ureteral and kidney stones can be managed in a similar fashion to adults. However in children, stones that are 4 mm or larger are unlikely to pass spontaneously. For this reason, children with a distal ureteral stone of 4 mm

or larger should be considered for ureteroscopic stone extraction (Fig. 21-3). Either prior placement of a ureteral stent for passive dilation or acute dilation of the ureterovesical junction may be necessary. Ureteral access sheaths can help minimize trauma associated with repeated scope passage. Small, rigid or flexible ureteroscopes can be used in conjunction with laser lithotripsy. Postoperative stenting is prudent in most cases.

Stone-free rates of between 77% and 100% have been reported. Reported complications include stone migration, bleeding, pyelonephritis, ureteral stricture, and ureteral avulsion. Ureteral injuries can be caused by the lithotripsy energy or mechanical injury associated with scope passage and stone manipulation. The incidence of vesicoureteral reflux after ureterovesical junction dilation is less than 1%.

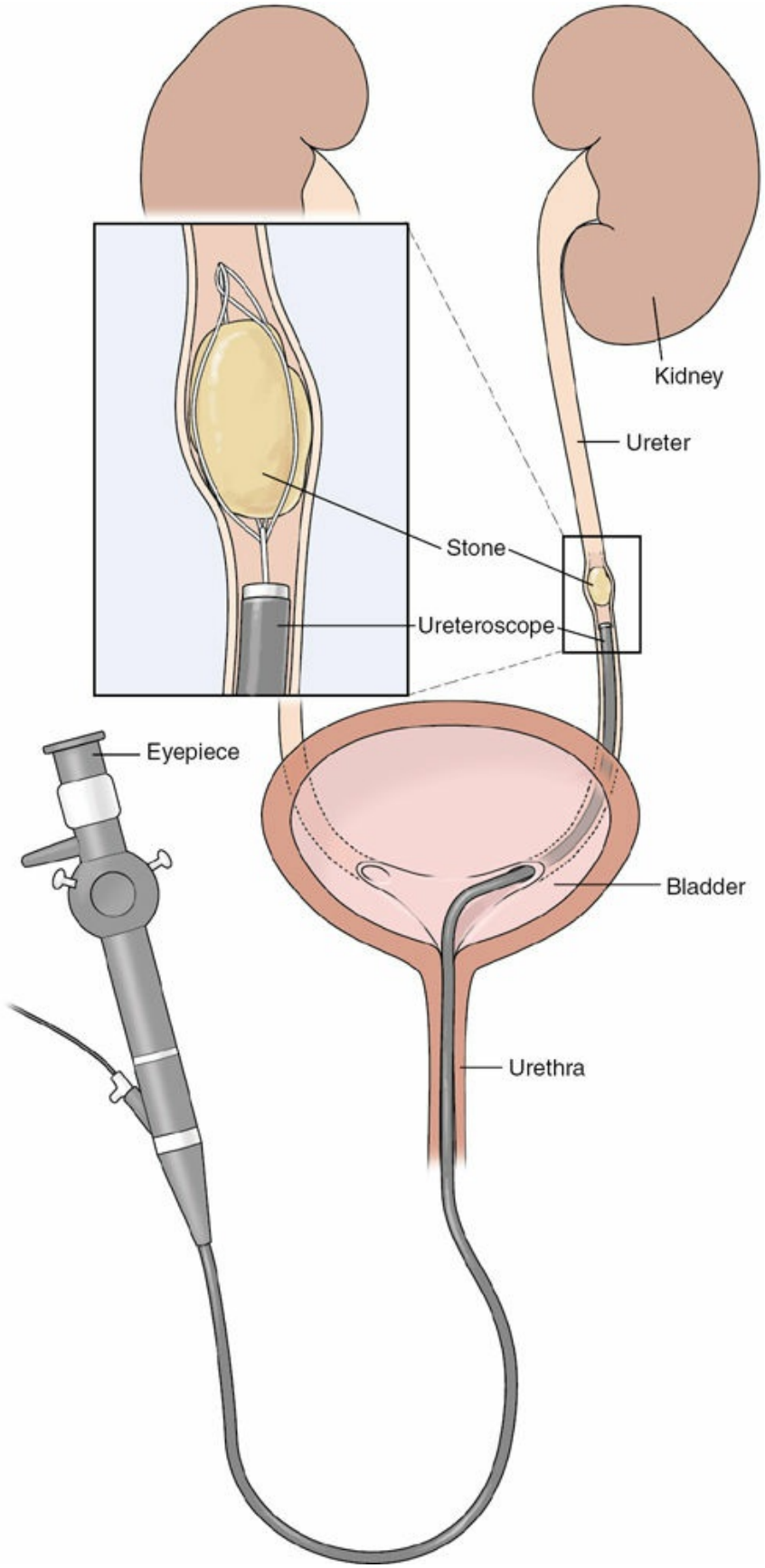
Kidney
Ureter
Stone
Ureteroscope
Eyepiece
Bladder
Urethra

Fig. 21-3 Patient undergoing ureteroscopic calculi extraction.

C. Percutaneous Nephrolithotomy

Percutaneous nephrolithotomy (PCNL) is useful in children with large upper tract calculi or very hard (cysteine or calcium monohydrate) stones. It is also useful for failed SWL and allows one to visualize radiolucent stones (e.g., uric acid stones). PCNL has been performed successfully in children of all ages (Fig. 21-4). Access to the kidney is achieved with a needle and guide wire using either ultrasound guidance and/or fluoroscopy through a small incision in the flank. A percutaneous tract is dilated to accommodate a sheath for which visualization instruments (nephroscopic/ureteroscope) can be placed directly into the kidney and/or ureter. These instruments will accommodate baskets, graspers, laser fibers, and/or high-energy ultrasonic probes to break up and remove calculi under direct vision.

Stone-free rates of 83% to 100% have been reported. Hematuria, sometimes requiring transfusion, urine leak, sepsis, and hypothermia have been reported. Bowel and pleural injury are also possible.

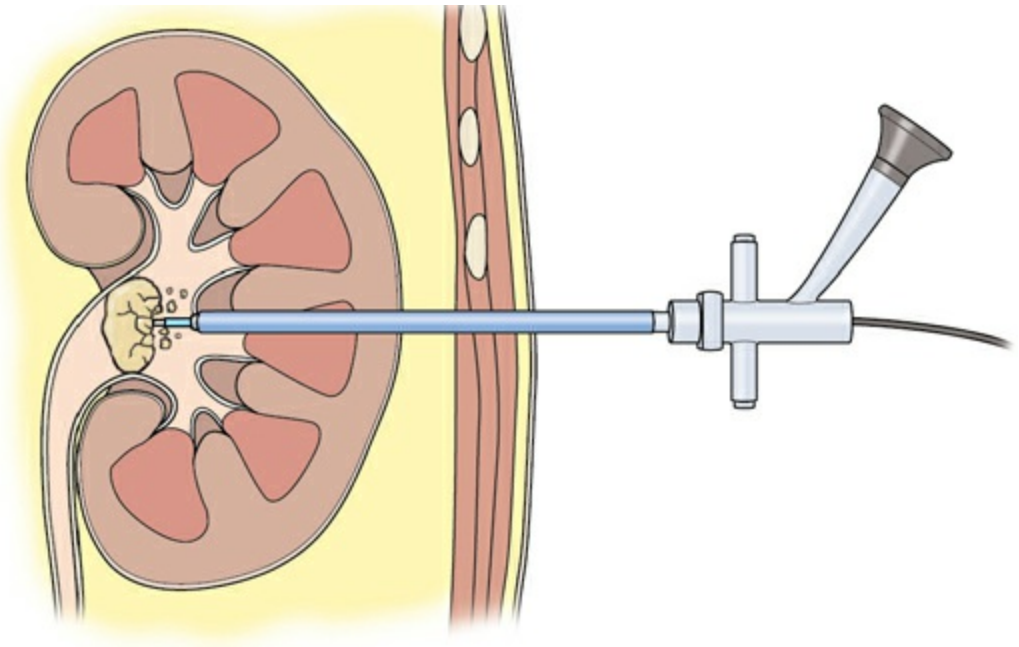

Fig. 21-4 Patient undergoing percutaneous calculi extraction.

D. Open Surgery or Laparoscopic Techniques

Open surgery is rarely necessary and is associated with longer recovery times. Laparoscopic and robot-assisted techniques are useful in children who have both a stone and an ureteropelvic junction obstruction, as combined stone removal and dismembered pyeloplasty are possible.

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22 Acute Kidney Injury

Paul R. Brakeman

I. DEFINITION

Acute kidney injury (AKI) is an abrupt reduction in renal function leading to an inability to excrete metabolic wastes and maintain proper fluid and electrolyte balance. AKI results in increased serum levels of creatinine, urea nitrogen and may result in increased serum potassium, increased serum phosphorus, metabolic acidosis, and/or oliguria. The presence and severity of AKI is defined based on elevation of serum creatinine and/or oliguria (see Table 22-1).

TABLE 22-1 pRIFLE Criteria

Stage	SCr-Based	Urine Output
Risk	>25% eCCl decrease	<0.5 mL/kg/h for 8 h
Injury	>50% eCCl decrease	<0.5 mL/kg/h
Failure	>75% eCCl decrease or eCCl <35 mL/min/1.73 m^2	<0.5 mL/kg/h for 25 h or <0.3 mL/kg/h for 12 h

Adapted from Fortenberry JD, Paden ML, Goldstein SL. Acute kidney injury in children: an update on diagnosis and treatment. *Pediatr Clin North Am* 2013 Jun;60(3):669–688.

II. CAUSES

The etiology of AKI is usually divided into three categories:

prerenal, intrinsic renal, and postrenal.

A. **Prerenal Azotemia**: Prerenal azotemia describes any condition in which blood flow to the kidneys is decreased. Causes of reduced renal blood flow include intravascular volume depletion, shock, sepsis, and heart failure. Prerenal azotemia is a common cause of AKI in intensive care units often related to hypotension or poor renal perfusion during complex surgery, frequently cardiac procedures with bypass. If reduced renal blood flow persists, then tubular cells may began to die in a process called acute tubular necrosis (ATN). It should be noted that histology rarely demonstrates necrosis in human renal injury, although the presence of tubular-cell casts on microscopic analysis of the urine is generally used to indicate the presence of ATN.
B. **Intrinsic Renal Causes**: The most common causes of intrinsic AKI (in order of frequency) are sepsis-related causes, ischemia, and toxins such as medications. While sepsis may cause renal dysfunction due to hypotension, inflammatory cytokines can cause direct renal injury and decreased renal capillary flow during sepsis. Other renal causes of AKI include glomerular disease such as acute glomerulonephritis (GN), renal vascular diseases such as hemolytic uremic syndrome (HUS), acute interstitial nephritis, and, in newborns, congenital anomalies of the kidneys. Pyelonephritis is an uncommon cause of AKI since it usually affects only one kidney.
C. **Postrenal AKI**: Postrenal AKI is caused by obstruction of the flow of urine at any level of the urinary tract.

III. CLINICAL FEATURES AND DIAGNOSIS

A. **History**: Many patients with AKI are asymptomatic and present only with alterations in laboratory findings. The patient and his or her medical record should be evaluated for recent fluid intake, last void, hematuria, stooling pattern, recent blood pressures (including intraoperative

blood pressures), heart rate, flank pain, malaise, rash, joint pain, fever, and recent medication exposures. A history of dehydration, sepsis, or previous complex surgery suggests prerenal azotemia. Exposure to tubular toxins such as amphotericin, IV contrast, or aminoglycosides, or drugs such as indomethacin that reduce renal blood flow suggest toxin-induced AKI. Bloody diarrhea with malaise suggests hemolytic uremic syndrome. Gross hematuria or bilateral flank pain suggests acute GN.

B. **Physical Examination**: Patients should be examined for altered mental status; hyper- or hypotension; tachycardia; face, pre-sacral (especially in the supine critically ill patient), or extremity edema; skin turgor; mucous membrane dryness; flank pain; abdominal mass; a palpable bladder; and rash. Poor skin turgor, tachycardia, and hypotension suggest prerenal azotemia. Commonly, children with AKI present with oliguria and signs of fluid overload such as edema and hypertension. Bilateral flank tenderness may indicate GN or interstitial nephritis. An enlarged bladder in a newborn suggests urinary obstruction such as posterior urethral valves.

C. **Laboratory and Imaging:** A complete blood count, urinalysis, and serum electrolytes, urea nitrogen, creatinine, calcium (including ionized calcium if the total calcium is low), phosphorus, and albumin should be obtained in all cases. If pyuria is present, a urine culture should be obtained. A renal ultrasound is frequently useful and should be obtained to evaluate for urine obstruction and/or structural abnormalities of the kidneys. Table 22-2 describes test results that can be used to differentiate causes of AKI.

TABLE 22-2 Laboratory and Radiologic Evaluation of AKI

Test Result	AKI Etiology

Urinalysis/microscopy	
Tubular casts	ATN
WBCs	Pyelonephritis, interstitial nephritis
Dysmorphic RBCs	AGN
Fractional excretion of sodium	
<1	Prerenal
>2	ATN, AGN
Elevated ASO, low C3	Postinfectious GN
Ultrasound	
Trabeculated bladder, hydronephrosis	Urinary obstruction
Increased echogenicity	AGN
Abnormal Doppler flow	Renal vessel thrombosis

ATN, acute tubular necrosis; WBCs, white blood cells; RBCs, red blood cells; AGN, acute glomerulonephritis; ASO, antistreptolysin O; GN, glomerulonephritis.

1. Urinalysis is the most important test in evaluating AKI. Mild proteinuria (1+ or less) is a nonspecific finding that occurs in many types of AKI. Severe proteinuria with or without hematuria and RBC casts is associated with intrinsic renal processes such as GN, vasculitis, HUS, or nephrotic syndrome. Pyuria is suggestive of pyelonephritis or interstitial nephritis.
2. The fractional excretion of sodium (FENa) {(urine [Na]/urine [Cr]) / (serum [Na]/serum [Cr])} is useful to distinguish prerenal azotemia from ATN. Prerenal azotemia is characterized by oliguria and concentrated urine with a high sodium concentration (greater than 40 mEq/L) and a low FENa, whereas ATN is characterized by low or normal urine volume and a dilute urine with a low sodium concentration (less than 20 mEq/L) and a high FENa. This measurement is not applicable to newborns who are unable to generate very concentrated urine.
3. Blood tests that can be used to diagnose various

forms of GN or vasculitis include compliment levels, anti-nuclear antibody (ANA) titer, anti-nuclear cytoplasmic antibody (ANCA) titer, and anti-streptolysin O (ASO) titer (to detect previous strep infection in cases of post- strep GN).

4. Ultrasound is the most important test for the diagnosis of congenital abnormalities or obstructive acute kidney injury as indicated by a finding of hydronephrosis. However, in the oliguric patient or early on in obstruction, no hydronephrosis may be detected despite the presence of postrenal obstruction. The finding of enlarged kidneys with bilateral increased echogenicity is consistent with medical renal disease such ATN, GN, interstitial nephritis, HUS, or renal vein thrombosis.

IV. TREATMENT

Many causes of AKI such as sepsis-related AKI, toxin-related AKI, or postinfectious glomerulonephritis are self-limiting diseases and have no specific treatment. The first step in the treatment of AKI is to reverse the cause of renal failure when possible. Next, steps are taken to maintain or correct fluid and electrolyte abnormalities. Finally, the kidneys should be protected from further toxic or ischemic insults during recovery from AKI. In cases of drug-induced ATN, the offending agent should be removed. In the case of obstructive renal failure, catheter drainage should be initiated and, if necessary, urgent surgical correction may be required. In the oliguric patient with presumed prerenal AKI, hydration with an isotonic solution should be started with 10 to 20 mL/kg over 30 to 60 minutes and continued until volume repletion is attained as indicated by the normalization of blood pressure, heart rate, skin turgor, and central venous pressure (CVP). To prevent further renal damage in AKI, drugs that detrimentally affect renal function such as angiotensin converting enzyme

(ACE) inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), and nephrotoxic antibiotics should be discontinued if possible.

A. **Fluids**: Children who are oliguric require salt and water restriction. Fluids should be restricted to calculated insensible water losses (35 mL/100 kcal/24h) adjusted for fever and measured urine output, usually given as D5/0.25% saline. Furosemide, 1 to 2 mg/kg IV may be tried to increase urine output, but in many cases it is ineffectual due to severely reduced glomerular filtration rate (GFR). There is no evidence that furosemide decreases the duration of ATN or changes other outcome measures of hospitalized patients with ATN. Fluid overload resulting in pulmonary edema that occurs despite fluid restriction is an indication for renal replacement therapy. In the pediatric intensive care unit (PICU) setting, fluid overload of more than 10% of total body volume is associated with a substantial increase in mortality.
B. **Hyperkalemia**: Intake of potassium should be restricted in most patients with AKI and potassium should be removed from IV fluids, particularly total parental nutrition. Mild hyperkalemia (serum K+ less than 6 mEq/L) is treated with IV furosemide (if the patient is furosemide responsive), IV sodium bicarbonate (1 mEq/kg) if the patient is acidotic, and/or with sodium polystyrene sulfonate (Kayexelate), 0.5 to 1 g/kg p.o. or 1.5 to 2 g/kg p.r. More severe hyperkalemia is treated with IV calcium gluconate, 100 mg/kg (maximum 2 g), over 10 minutes, sodium bicarbonate, 1 to 2 mEq/kg, over 15 to 30 minutes, 50% dextrose in water 1 mL/kg and insulin, 0.15 u/kg, over 15 to 30 minutes, and with sodium polystyrene sulfonate as above. The patient with severely elevated potassium should be assessed for the presence of peaked T waves on electrocardiogram (ECG).
C. **Hypocalcemia**: In AKI, reduction of renal excretion of

phosphorus results in hyperphosphatemia that leads to hypocalcemia. Hypocalcemia is exacerbated by a reduced ability to hydroxylate vitamin D in AKI. Hypocalcemia severe enough to result in a positive Chvostek or Trousseau sign or tetany (usually lower than 6.0 mg/dL) is treated with IV calcium gluconate 100 mg/kg (maximum 1 g) every 6 hours. Serum phosphorus should be reduced by treating with a phosphorus binding agent such as sevelamer with meals and snacks. Hemodialysis is minimally effective in reducing serum phosphorus levels.

D. **Acidosis**: Severe acidosis (serum pH less than 7.2 or serum bicarbonate level less than 16 mEq/L) is initially treated with sodium bicarbonate, 1 to 3 mEq/kg IV, over 30 to 60 minutes followed by slow correction with IV or p.o. sodium bicarbonate over 24 hours to a goal serum level of 20 mEq/L. Maintenance therapy with sodium bicarbonate is 1 to 3 mEq/kg/day IV or p.o. and thus correction of acidosis requires providing 1 to 3 mEq/kg/day of sodium bicarbonate in addition to the amount required to achieve correction. Correction of acidosis exacerbates hypocalcemia, thus treatment of hypocalcemia should precede or accompany treatment of acidosis.

E. **Anemia**: Severe anemia (hematocrit less than 20%) is treated with packed red blood cells. Transfusion can exacerbate hypocalcemia, hypervolemia, and hypertension and should be given slowly.

F. **Azotemia**: In AKI increased catabolism due to fever, fasting, and stress aggravates elevated blood urea nitrogen (BUN) levels. Adequate calories (75% to 100% of the recommended daily allowance [RDA]) and restriction of protein intake to RDA levels can decrease the accumulation of BUN. Severe azotemia (usually greater than 100 mg/dL) can lead to symptoms of uremia including bleeding, malaise, encephalopathy (in severe azotemia), nausea, and vomiting which are indications to initiate dialysis. In the absence of these uremic symptoms,

dialysis in the setting of AKI can be delayed until BUN exceeds 100 to 120 mg/dL.

G. **Hypertension**: Hypertension in AKI is usually caused by fluid retention and can be treated with salt and water restriction and/or diuresis with furosemide, 1 to 2 mg/kg in the diuretic responsive patient. Inability to respond to these therapies suggests the presence of increased plasma renin levels that can result from AKI. Children unresponsive to fluid restriction or diuresis can be treated with amlodipine, 0.1 to 0.5 mg/kg/day p.o. divided q 12 or 24 hours. For patients unable to take oral medications, hypertension can be treated with IV hydralazine or labetalol. Severe hypertension associated with end-organ damage such as seizure, pulmonary edema, or stroke constitutes a hypertensive emergency and merits transfer to a pediatric intensive care unit for aggressive intravenous blood pressure control.

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23 Chronic Kidney Disease

Paul R. Brakeman

I. DEFINITION

Chronic kidney disease (CKD) is a persistent reduction in renal function lasting for more than 3 months that results in a variety of clinical signs and symptoms and multiple metabolic, hormonal, and organ system abnormalities. CKD is classified by severity (Table 23-1) with the most severe form being kidney failure or end stage renal disease (ESRD).

TABLE 23-1 Classification of Chronic Kidney Disease

GFR Category	eGFR/GFR (mL/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased
G3A	45–59	Mildly to moderately decreased
G3B	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

GFR, glomerular *filtration rate.*

Adapted from KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013;3(1):1–150.

II. PREVALENCE

The prevalence of chronic kidney disease varies significantly

between studies and is in the range of 25 to 50 per million children.

III. CAUSES

The most common causes of CKD in North America are listed in Table 23-2. The most common cause of CKD in children in North America are congenital anomalies of the kidney and urologic tract known as CAKUT and represent nearly half of all cases of CKD in children. In younger patients, congenital anomalies are more common while in adolescent patients the various forms of glomerulonephritis are the most common cause of CKD.

TABLE 23-2 Most Common Causes of CKD in North America

Causes	Percentage of Total
CAKUT	49.2
Obstructive uropathy	20.7
Dysplasia/hypoplasia	17.3
Reflux nephropathy	8.4
Prune belly	2.7
FSGS	8.7
Glomerulonephritis	8.4
Cystic diseases	4.0
Renal infarct	2.2
Hemolytic uremic syndrome	2.0
SLE	1.6
Cystinosis	1.5
Chronic pyelo/interstitial nephritis	1.4
Henoch-Schonlein purpura	1.3

CAKUT, congenital anomalies of the kidneys and urinary tract; FSGS, focal segmental glomerulosclerosis; SLE, systemic lupus erythematosus.

Adapted from the North American Pediatric Renal Transplant Cooperative Study, Annual Report, 2008.

IV. PATHOGENESIS

As CKD progresses, individual nephrons are lost and the total glomerular filtration rate (GFR) decreases. To compensate, the remaining nephrons increase the fraction of filtrate that is excreted as urine. Thus, substances that depend on glomerular filtration for excretion such as urea nitrogen accumulate while substances such as salt, potassium, and water may remain in homeostasis until the final stages of CKD. This is specifically true in the case of CKD resulting from congenital obstructive uropathy or hypoplastic/dysplastic kidneys in which a patient may reach end stage renal disease with a normal urine output and near normal excretion of sodium and potassium.

V. CLINICAL MANIFESTATIONS

Many of the same biochemical abnormalities occur in CKD and ARF; however, in CKD persistence of these abnormalities results in organ system pathology such as renal osteodystrophy.

VI. DIAGNOSIS

A. **History:** A patient with CKD should be evaluated thoroughly for a family history of renal failure and hearing loss suggestive of hereditary nephritis (Alport syndrome), cystic kidney disease, and family members receiving dialysis and/or renal transplantation indicating other heritable causes of CKD. A CKD patient should be questioned for a history of abnormal bladder emptying, constipation, recurrent urinary tract infections, vesicoureteral reflux, or meningomyelocele any of which could suggest obstructive uropathy as a cause for CKD. The patient should be evaluated for a history of proteinuria, hematuria, flank pain, or edema consistent with chronic glomerulonephritis (GN) and for previous episodes of skin rashes, fever, adenopathy, or arthralgias

consistent with systemic lupus erythematosus (SLE) or a vasculitis. Many times the absence of a previous history of symptoms or renal disease is indicative of CKD due to congenital anomalies of the kidneys such as hypoplasia/dysplasia or medullary cystic disease.

B. **Physical Examination:** The infant with CKD should be examined for enlarged kidneys indicative of hydronephrosis or autosomal recessive polycystic kidney disease; enlarged bladder indicative of obstructive uropathy; and abnormal bony structure of the lumbar spine indicative of meningomyelocele associated with neurogenic bladder. Older patients should be evaluated for hypertension; rash or arthralgia indicative of SLE; and hearing loss consistent with hereditary nephritis.

C. **Laboratory and Imaging**

1. Urinalysis: Hematuria with moderate to severe proteinuria is suggestive of chronic GN or hereditary nephritis. Milder proteinuria with or without mild hematuria is more typical of congenital dysplasia or obstructive uropathy.
2. Blood: Complete blood count, iron studies, serum electrolytes, urea nitrogen, creatinine, calcium (including ionized calcium if the total calcium is low), phosphorus, serum alkaline phosphatase, parathyroid hormone level, and albumin should initially be obtained and monitored in patients with CKD.
3. Imaging: Renal ultrasound is the most important imaging modality in diagnosing congenital anomalies of the kidneys, obstruction, and scarring due to chronic pyelonephritis. In children who present with advanced renal failure and no previous history of renal disease, the kidneys are often small and echogenic on ultrasound. This appearance is nondiagnostic; however, in such patients a voiding cystogram may show vesicoureteral reflux suggesting obstructive uropathy as the etiology of their renal

failure. The absence of reflux in such a patient is nondiagnostic since reflux may resolve after scarring has already occurred.

D. **Biopsy:** Renal biopsy is used to diagnose the many forms of glomerulonephritis, interstitial nephritis, and hereditary nephritis. Rarely, it establishes a diagnosis of medullary cystic disease. In children with small kidneys by ultrasound, biopsy is not usually performed because small kidneys often exhibit only nonspecific scarring on pathologic specimens.

VII. MANAGEMENT

Most of the signs, symptoms, and biochemical abnormalities occurring in CKD are the same as those occurring in acute kidney injury (AKI), although more severe abnormalities are indicative of CKD rather than AKI, with a slow onset allowing the patient to adjust to the severe metabolic abnormalities with limited symptoms. The most important clinical manifestations of CKD are listed below. Intractable hyperkalemia, persistently elevated blood urea nitrogen (greater than 100), and pulmonary edema are late findings in CKD and indicate the need to initiate dialysis.

A. **Fluid Retention:** Children with CKD who are oliguric require sodium restriction to 2 g of sodium per day for older children and adjusted downward based on the energy requirements of children relative to those of adults. Furosemide, 1 to 2 mg/kg/dose orally two to three times per day, may also limit edema in the furosemide responsive patient.

B. **Hypertension:** Many patients with CKD are hypertensive and hypertension can accelerate the progression of CKD. Common treatments for hypertension include:
   1. Salt restriction, as above.
   2. Angiotensin converting enzyme (ACE) inhibition: Enalapril, 0.1 to 0.5 mg/kg/day in two divided doses.

In-vitro data in animals and extrapolation of data from patients with diabetes mellitus and SLE indicate that the use of ACE inhibitors in patients with proteinuria and/or renal insufficiency may provide some renoprotection and slow the progression of CKD. Because of the side effects of hyperkalemia and reduced GFR, serum electrolytes, blood urea nitrogen (BUN), and creatinine (Cr) must be monitored in patients receiving ACE inhibitors.

3. Amlodipine, 0.1 to 0.5 mg/kg/day in one to two divided doses.
4. Furosemide, 0.5 to 1 mg/kg twice a day.
5. For those patients not adequately controlled with vasodilatory medication such as calcium channel blockers or ACE inhibition, addition of clonidine or a beta-blocker such as metoprolol is indicated.

C. **Renal Osteodystrophy**

1. Restrict phosphorus to 15 mg/g of protein per day.
2. Sevelamer, 400 to 1600 mg with meals and snacks, to bind phosphorus in the gut and maintain a normal serum phosphorus level.
3. Active vitamin D: calcitriol, 0.25 to 1.0 mcg/kg/day in older children is used to suppress inappropriately high parathyroid hormone levels. In addition, 25-OH vitamin levels are maintained in the normal range with oral supplementation as low 25-OH vitamin D levels are associated with increased mortality in patients with CKD.

D. **Anemia:** When the hematocrit is lower than 30%, erythropoietin is started, 100 units/kg one to three times per week depending on severity of CKD with a goal hematocrit of 30% to 35%. Iron is given as adjunctive therapy with erythropoietin as patients with CKD often demonstrate malabsorption of iron and iron deficiency. Transfusions are avoided when possible to prevent sensitization to antigens that might complicate transplantation and are given only if the child is

symptomatic or has a hematocrit less than 18% to 20%.

E. **Acidosis:** Sodium citrate solution, 1 to 3 mEq/kg/day in three divided doses is given to infants and young children and sodium bicarbonate, 1 to 2 mEq/kg/day in three divided doses is given to older children.

F. **Azotemia:** High levels of BUN (greater than 80 mg/dL) can cause anorexia, fatigue, and other uremic symptoms. Protein restriction to the recommended daily allowance (RDA) minimum can help prevent the development of azotemia. Protein restriction below the RDA interferes with growth in children. In humans, protein restriction has proven to be of only marginal benefit in delaying the progression of CKD.

G. **Nutrition and Growth:** Anorexia related to uremia frequently causes inadequate calorie intake in CKD. Inadequate calorie intake is treated with supplementation with carbohydrates and fats while maintaining the protein restriction described above. In school-age or adolescent patients, appetite stimulants such as cyproheptadine or megestrol acetate may be used to increase calorie intake. In younger children and infants, inadequate calorie intake can detrimentally affect brain growth and development causing decreased head circumference and delayed developmental milestones. Frequently, gastrostomy feedings are necessary in younger patients with severe CKD to achieve adequate growth. Acidosis, anemia, and renal osteodystrophy can also limit growth. Patients who do not achieve normal linear growth despite adequate calorie intake, correction of acidosis, and the absence of renal osteodystrophy are treated with recombinant growth hormone, 0.05 mg/kg/day.

H. **Imaging with Intravenous Radiocontrast Dye:** There is significant risk of contrast-induced AKI in patients with renal insufficiency. There have been several studies in adults indicating that the administration of oral N-acetylcysteine and IV hydration before and after the procedure can reduce the number of patients that have a

rise in creatinine following CT scans and coronary angiography. A typical protocol for adults is to hydrate with 1 cc/kg/h of 0.9% normal saline for 12 hours before the procedure and for 12 hours after the procedure and to give N-acetylcysteine, 600 mg p.o. every 12 hours starting one day prior to the procedure for a total of four doses—two before the procedure and two after the procedure. Given the data in adults it is reasonable to use this protocol for adolescents or larger children receiving IV contrast with a creatinine greater than 1.5 mg/dL or creatinine clearance less than 50 mL/min. In the outpatient setting, IV hydration can be given the day of the procedure, 5 to 10 cc/kg of 0.9% normal saline over 1 to 2 hours with careful monitoring for signs of hypertension or pulmonary edema.

I. **Dialysis and Transplantation:** The indications for initiating chronic dialysis in a patient with CKD are: lethargy, nausea, or vomiting due to uremia; BUN greater than 100 persistently; GFR less than 8 to 10 mL/min/1.73 m^2; persistent hyperkalemia; or pulmonary edema. Dialysis can either be undertaken as hemodialysis, typically three times per week, or daily peritoneal dialysis which can be administered at home either manually throughout the day (continuous ambulatory peritoneal dialysis— CAPD) or continuously during the night using a cycling machine (continuous cycling peritoneal dialysis —CCPD). Both forms of dialysis provide only approximately 15% of normal renal function; therefore, dialysis patients still experience many of the complications of CKD. The optimum treatment for children with ESRD is transplantation. The child with CKD should be evaluated for transplantation before reaching ESRD. If a suitable living donor can be identified, the transplant can be performed before the child develops significant symptoms of CKD. When there is no living donor, the child is placed on a waiting list to receive an allograft from a deceased donor. Because of

the shortage of organs, most children on the deceased donor waiting list require some type of dialysis before receiving their transplant.

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24 Pediatric Renal Transplantation

Gerald C. Mingin and Jeffrey A. Stock

I. OVERVIEW

In children with end stage renal disease (ESRD), renal transplantation represents the current optimal standard of care for renal replacement. Despite the effectiveness of hemodialysis and peritoneal dialysis, even with the addition of recombinant erythropoietin and growth hormone for the prevention of anemia and lack of growth to the armamentarium, neither of these options has proven more effective than renal transplantation. The success of renal transplantation in children has steadily improved over the past three decades.

The North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) was established in 1987 to collect and distribute clinical data regarding pediatric transplantation in North America. One-year graft survival (GS) from living related donors (LRD) has increased from 91% (1987 to 1995) to 96.4% (2007 to 2013), while cadaver donor survival has increased from 81% to 95.8% during the same interval. In fact, most recent patients appear to be exhibiting equal 1-year allograft survival rates, regardless of whether the donor source of the allograft was living or cadaveric. This is of added importance since allograft half-lives, that is, long-term transplant kidney survival, directly correlate well with 1-year survival rates. In the 2003 to 2010 cohort, 5-year allograft survival for LRD was 84.3% and 78%

in the deceased donor cohort.

Between 2008 and 2014 the incidence of ESRD has been decreasing annually in the United States. In 2014, a total of 1,398 children were diagnosed with new onset ESRD, which was 6% less than in 2013. In 2014, 1,312 children were waitlisted for a kidney transplant (896 listed for the first time and 425 listed for repeat transplant). Since 1997 there has been a decrease in the median wait time for those listed for their first transplant. The median waiting time for children receiving their first kidney transplant has ranged between 150 and 220 days. Children receiving a repeat transplant have been waiting 3 to 4 times longer than those awaiting their first transplant. A total of 1,018 children received a kidney transplant in 2014. Prior to 2005, the source of kidney grafts in pediatric transplant recipients was most commonly from living donors. There has been a steady decline in the number of children receiving living donor kidneys since 2009. In 2014, living donors accounted for 40% of kidney transplants, which is a 21% decrease since 2009.

It has been recognized that preemptive transplantation decreases the morbidity associated with chronic dialysis, thus potentially improving physical health, statural growth, and mental well-being. During 2010 to 2014, 36% of children received a kidney transplant within the first year of being diagnosed with ESRD. In recognition of the overt benefits of transplantation, pediatric patients with ESRD are given special consideration in the allocation of organs; despite this, waiting times remain long for the fixed source of cadaveric organs and this problem is not likely to be solved in the near future.

Currently increased graft survival is dependent on identifying the most appropriate donor recipient characteristics while employing ongoing improvements in immunosuppressive therapy. This chapter highlights some of

the recent and important changes in pediatric renal transplantation.

II. ETIOLOGY AND DEMOGRAPHICS

The etiologies of renal failure in pediatric patients differ significantly from that of adult patients (older than 18 years of age) in that urologic etiologies and/or comorbidities can be found in 30% to 40% of children compared to less than 10% of adults. The major urologic conditions associated with ESRD in pediatric patients requiring renal replacement include obstructive uropathy (16%), hypoplastic/dysplastic kidney disease (15%), and reflux nephropathy (5%). The most common medical causes of ESRD include: focal glomerular sclerosis, membranous nephropathies, autoimmune disease, metabolic defects, diabetes, and tumor.

While these etiologies have remained relatively constant, the demographics have shifted significantly. This is most pronounced in the ethnic mix, where Caucasian recipients have decreased. In turn, the number of African-American and Hispanic patients has increased from 28% in 1987 to almost 40% in 2007. In 2013, 55% of pediatric kidney recipients were Caucasian down from 72% in 1987.

III. SELECTION OF RENAL DONORS

Although the short-term survival of deceased donor (DD) allografts have been shown to be nearly equal to that of LRD allografts, the use of a LRD or LURD (living unrelated donor) is still preferable in children because long-term graft survival is superior. With live donors, families are better able to plan and prepare for the surgery; in addition there is a potential psychological benefit to the recipient knowing the source of the organ and to the donor by virtue of being a good Samaritan. However, this must be weighed against the

knowledge that if the graft is lost, there can be considerable anguish, grief, and guilt from both the donor and recipient. Recently, computerized matching algorithms have been designed to identify maximal sets of donor/recipient pairs, generally forming “chains” from large sets of able donors who are either not compatible with their intended recipient or, in some cases, when greater compatibility can be achieved through this “donor” exchange pool.

Donor-recipient compatibility is based on several immunologic factors. The “cytotoxic crossmatch,” in which donor lymphocytes are mixed with recent recipient sera, is performed prior to any transplant. A positive crossmatch where recipient preformed reactive antibodies attack specific antigens on recipient cells is a contraindication to transplantation as it will lead to hyperacute (immediate) rejection. The matching process now includes more sensitive means of predicting rejection as well, including detection of low-level incompatibility by flow cytometry. Donor-specific antibodies (DSA) can now be detected with high sensitivity by immunofluorescence.

The two primary antigen systems associated with graft rejection are the ABO and human leukocyte antigen (HLA) systems. Similar to blood transfusions, type O represents the universal blood donor while type AB represents the universal recipient. Hence an appropriate match should be assured to avoid hyperacute rejection. The Rh status appears to be a minor antigen system that does not influence the risk of rejection. The short-term and long-term survival of a transplanted kidney appear to be related with HLA compatibility at the A, B, and D (DR) loci primarily, though other loci are clearly relevant and figure in some matching decisions if not to define basic compatibility. Ideally a “zero antigen mismatch” is desired. In a LRD from parent to child

there is at worst a 1 haplotype or up to 3 HLA mismatch. An identical twin should be a 2 haplotype (same maternal and paternal alleles)/0 mismatch donor; consanguineous parents may also share full haplotypes with their offspring. In a sibling group, there is a 50% chance of sharing 1 haplotype (1 maternal or 1 paternal) and a 25% chance of being either a full haplotype or totally mismatched. Clearly in the DD the chance of obtaining a perfect match is far less due to the HLA distributions in various populations and ethnic/cultural groups.

All donors are screened for systemic infections such as AIDS and hepatitis as well as malignancy (with the exception of some primary brain tumors). In rare individual cases, the criteria have been expanded to include kidneys from non-heart-beating donors, donors younger than 5 years or older than 60 years and in exceptional cases, a kidney from a deceased donor with diabetes or hypertension. Among adults, some recipients with hepatitis or HIV may elect donors with the same infection due to the availability of highly effective antiviral therapy. Any LD should be healthy, free of systemic illness or malignancy, and be freely willing to donate. The perioperative donor risk is small with a mortality rate between 0.03% and 0.06%. Long-term data have substantiated that while the attributable risk of ESRD or other significant long-term morbidity or mortality from becoming uninephric is nonzero, the absolute risk is extremely low and it is considered acceptably safe. Live donors may experience age-related development of hypertension sooner than they would have otherwise, and there is a somewhat higher risk of developing gout, pregnancy-induced hypertension, and preeclampsia.

IV. PRETRANSPLANT RECIPIENT PREPARATION

A. Metabolic Diseases

The activity of systemic diseases such as systemic lupus

erythematosus and vasculitis require a stable and quiescent state prior to transplantation. Often times, the autoimmune responses in these diseases can be controlled with the same immunosuppression required for antirejection therapy and maintenance.

Metabolic and systemic diseases such as atypical hemolytic uremic syndrome (HUS), cystinosis, and primary hyperoxaluria require adequate medical therapy prior to transplantation. Specific therapy for these diseases exist, though in some cases, particularly primary hyperoxaluria type 1 with infantile ESRD, combined liver-kidney transplantation may be considered. Other specific diseases such as autosomal recessive polycystic kidney disease (ARPKD) and other "ciliopathies" that potentially affect both kidney and liver require specific evaluation for potential liver transplantation as well. Patients with cancer (such as bilateral Wilms tumor) require a disease-free waiting period before immunosuppression.

B. **Upper Urinary Tract**

Clinical conditions that require pretransplant nephrectomy are few and far between. However, consideration for nephrectomy(ies) includes those children who have severe polyuria with electrolyte wasting and patients with significant proteinuria. Polyuria, dehydration and electrolyte disturbances, and importantly, a reduced circulating volume can lead to a hypercoagulable state. It should be emphasized that the child often receives a larger donor kidney that requires a significant cardiac output and perfusion pressure. Thus a low recipient volume status can precipitate thrombosis, a surgical complication more prevalent in pediatric patients than adults, and often thought to be technical in etiology.

As opposed to years gone by when routine nephrectomies were performed in patients with a history of obstructive uropathy and vesicoureteral reflux, this is rarely an indication today, unless the patient is prone to

relapsing recurrent infections that can be attributed to the kidney. Renal hypertension that cannot be controlled with medication may be considered a rare indication for nephrectomy in order to improve blood pressure control. In children who have an associated predisposition to the development of malignant renal neoplasms, such as those with Denys-Drash syndrome, nephrectomies should be performed as these tumors tend to occur early in life.

C. **Lower Urinary Tract**

As alluded to earlier, a substantial minority of children with ESRD have associated urologic anomalies that may have contributed to native kidney loss and potentially might negatively impact an allograft. Investigation must be individualized to assure that the lower tract is hospitable to a new kidney. The goal in all cases is to ensure that the bladder serves its two primary functions: storage of urine (at an adequate capacity with pressures less than 35 cm of water) and emptying (completely and reliably). Patients with a history of posterior urethral valves, neurogenic bladder, urethral strictures, and anatomic anomalies such as bladder exstrophy, should be scrutinized closely. Depending on the individual age and other parameters, urologic investigation may range from nothing, to uroflow with pre- and postvoid bladder scans, all the way to videourodynamics.

Clean intermittent catheterization (CIC) can be performed safely via the urethra or using the Mitrofanoff technique (through a continent stoma) when spontaneous voiding is not possible. In addition if anticholinergic medications are insufficient in controlling the “inhospitable” bladder, then augmentation cystoplasty will be required. Occasionally the anuric patient will have a defunctionalized bladder. If the bladder was normal prior to the onset of anuria, then the bulk of these bladders will stretch and contract normally after successful transplantation. If there is a doubt, bladder cycling using CIC or suprapubic catheter installation of saline can be

used to test the distensibility and emptying parameters of the bladder. In patients with a preexisting continent cutaneous diversion, reimplantation of the transplant ureter can be performed into these systems. In the case of an incontinent diversion, conversion to a continent catheterizable system can be performed electively either pretransplant or posttransplant when the child is stable with regard to renal function and is on maintenance immunosuppression.

D. **Blood Transfusions (BT)**

It is well known that renal failure leads to a decrease in the production of erythropoietin and subsequent anemia in patients with ESRD. Early on it was noted that patients who received red cell transfusions had fewer episodes of rejection. As a result, in many centers it became routine for potential recipients to receive multiple transfusions and in the case of the LRD, multiple donor-specific transfusions. However, a number of these patients went on to develop unacceptably high levels of anti-HLA antibodies, which delayed or even precluded subsequent transplantation. Due to the use of recombinant erythropoietin the need for transfusion has decreased dramatically from a high of 83% in 1987 to 45% in 1999. Most recent data suggests that with current immunosuppressive protocol, the risk of transfusions and their associated hypersensitivity outweigh their potential immunologic benefits and hence, **donor specific transfusions** should be abandoned. should be abandoned.

V. IMMUNOSUPPRESSIVE AGENTS

The improvement in graft survival over the last several years is likely due to modern immunosuppression, focus is now on optimizing immunotherapy in order to decrease potential recipient side effects while maintaining or even improving graft survival, hence the focus is now on. Hyperacute rejection is preventable in virtually all cases by assuring a negative

crossmatch. There are two other important types of rejection. Acute rejection, however, can occur anytime after the graft is placed. The most common cause of graft loss now is chronic transplant glomerulopathy. This term encompasses many processes including chronic low-level antibody-related activity as well as the cumulative effects of initial surgical injury, medication-related effects, and in some cases disease recurrence, viral infection, or UTI. Graft loss from any of these processes is prevented by immunosuppresion. All immunosuppressives carry increased risk of infection and of posttransplant lymphoproliferative disorders (PTLD). The optimal immunosuppressive agent(s) is still elusive. However, in many cases, the level of immunosuppression can be adjusted based on the donor/recipient match. Immunosuppressive agents can be broadly grouped into those used for induction, those used for maintenance, and those used for anti-acute rejection therapy.

A. **Corticosteroids**

Corticosteroids have a wide range of nonspecific and specific anti-inflammatory effects on cell-mediated immunity and have been a mainstay in the immunosuppression armamentarium for almost five decades. They are employed for induction, maintenance, and when administered in high doses (pulses), in anti-acute rejection protocols as well. Although it has been standard practice to use steroids in children, their side effects can be severe. Some of the more common problems seen with steroid use include cushingoid habitus, susceptibility to infection, impaired wound healing, and growth suppression. In recognition of these deleterious effects, lower steroid dose protocols and alternative day dosing verses replacement with daclizumab appear to have no deleterious effect on the acute rate of rejection. Protocols using rapid steroid

withdrawal (within days of the transplant) are in place in many centers with good results.

B. **Interleukin-2 Inhibitors/Blockers**

The calcineurin inhibitors cyclosporine and tacrolimus are sister peptides of fungal origin that are utilized in induction and maintenance. Cyclosporine inhibits T-cell response by binding to cellular proteins called cyclophilins. This complex then blocks the movement into the nucleus of those transcription factors required for interleukin-2 (IL-2) production. The introduction of cyclosporine or cyclosporin A (CyA) in the 1980s, when it failed in its initial development as an antibiotic but demonstrated unique immunosuppressive properties, essentially ushered in the modern era of transplantation and indeed has been responsible for the explosive expansion in multi-organ transplantation. Tacrolimus is produced from the fungal species *Streptomyces tsukubaensis*. However, its binding site is distinctly different from cyclosporine. Tacrolimus complexes are monitored by measuring serum levels to keep a balance with FK binding protein to inhibit T-cell-derived lymphokines such as IL-2. The use of cyclosporine is associated with nephrotoxicity, hepatotoxicity, hypertension, hirsutism, gingival hyperplasia, risk of posttransplant diabetes, susceptibility to infection, and increased risk of malignancy. Tacrolimus has a similar set of side effects but not gingival hyperplasia. Tacrolimus, in addition to being effective in inducing graft tolerance, appears to be just as successful in the absence of steroids when used as monotherapy. Since both of these drugs are metabolized by the cytochrome P-450 system, it is important to be aware of those drugs which can induce or inhibit metabolism of cyclosporine and tacrolimus. Their levels are monitored to keep a balance of immunosuppression on the one hand and toxicity on the other by measuring serum levels.

A second group of drugs used for induction are

antibodies directed to the interleukin-2 receptor. Basiliximab blocks the alpha chain of the IL-2 receptor whereas daclizumab (presently not available in the United States for transplantation) acts at the alpha chain of that receptor. Both of these antibodies have been shown to significantly reduce the incidence of biopsy-proven acute rejection. They also have the added benefit of being well tolerated despite significant side effects.

C. **Antimetabolites**

Azathioprine is an antiproliferative agent, a prodrug of 6-mercaptopurine. Once metabolized its derivatives inhibit purine synthesis, which prevents gene replication and in turn inhibits antibody formation. Myelosuppression is a major side effect of this drug and it is rarely used anymore due to the introduction of more specific agents. Mycophenolate mofetil (MMF) and mycophenolic acid interrupt purine metabolism in B and T lymphocytes and have replaced azathioprine in most protocols. The side effects include hematologic and gastric problems, in particular neutropenia, thrombocytopenia, diarrhea, nausea, and vomiting. Viral infections are also a common side effect of these drugs.

Sirolimus and everolimus are mechanistic target of rapamycin (mTOR) inhibitors, working to inhibit progression through the cell cycle, making these generally "antiproliferative" and effective by inhibiting the cytokine-mediated proliferation of T and B lymphocytes that would lead to rejection. These agents are not frequently used in the perioperative period due to some concern that they may inhibit wound healing, itself a proliferative process. Among patients with concurrent tumors, mTOR inhibitors may be preferred in some cases for antitumor properties.

D. **T-Cell Antibody Therapy**

OKT3 is a monoclonal antibody that binds to the lymphocyte–CD3 complex and antithymocyte globulin (Atgam), a polyclonal horse-derived antilymphocyte

globulin. Another agent, rabbit antithymocyte globulin (Thymoglobulin), has also been shown to be effective in the depletion of T lymphocytes and is the most common of these antibodies utilized currently. These parentally administered anti-antibody preparations are associated with infusion-related side effects that include fever, chills, nausea, and hypotension. Premedication with acetaminophen, corticosteroids, and diphenhydramine is therefore recommended. Alemtuzumab is another T-cell-depleting antibody but it is synthetically derived and less prone to severe allergic response. The potential morbidity due to their potential immunosuppression is related to extreme reduction in circulating active lymphocytes, with resultant risk of infection and PTLD; they are utilized primarily for induction and the treatment of acute rejection (not long-term maintenance).

Newer agents such as belatacept, newer calcineurin inhibitors like voclosporin, and other agents still in development (anti-CD40 monoclonal antibody) continue to be sought after; agents like rituximab, bortezomib, and eculizumab may have occasional roles in the treatment of acute rejection in certain patients.

E. **Typical Immunosuppressive Regimens**

Although protocols differ depending on the institution, the following is fairly representative. An induction agent with a lymphocyte-depleting therapy or anti-IL-2 receptor antibody is used in most centers. Maintenance therapy is accomplished in most cases using tacrolimus or cyclosporine and MMF. Corticosteroids are used in many centers initially; some patients are maintained on daily doses indefinitely, others progress to treatment every other day, and in some centers, rapid steroid withdrawal is utilized. Rapamycin may be used in patients intolerant of tacrolimus or cyclosporine. Belatacept is uncommonly used and only in patients who fail other classes; it should not be used in recipients without immunity to Epstein-Barr virus (EBV) as the risk of PTLD is considered very

high.

Acute rejection is treated with pulse steroids and/or antibody preparations such OKT3, antilymphocyte globulin, or antithymocyte globulin. The morbidity of single as well as repeated treatments of multiple rejection episodes must be assessed with the philosophy that the patient is more valuable than the graft survival and that there is the fallback of dialysis if an allograft is lost.

VI. GRAFT LOSS

Graft loss may be due to hyperacute rejection, acute rejection, chronic rejection, vascular thrombosis, technical mishaps, and recurrent disease. Acute rejection is the second leading cause of allograft loss as well as being the biggest contributor to chronic rejection. Acute rejection is increased in African-Americans, in HLA mismatch, and with a lack of induction therapy. Silent rejection has become an important issue in children where it is postulated that because of the larger adult kidney, acute rejection requires a greater amount of time to become clinically apparent.

Chronic rejection is still the primary cause of graft failure, accounting for 30% to 40% of allograft loss. Even so, more recent analysis of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) database has shown that the incidence of chronic rejection has fallen significantly since 1987. This is most likely due to improvements in immunosuppression leading to a decrease in acute rejection. This improvement may also be related to improved renal storage methods that promote early graft function.

Vascular thrombosis is the third leading cause of graft failure and, according to the NAPRTCS registry, is responsible for graft loss in 11.6% of children. The following patients have an increased risk for thrombosis: peritoneal dialysis patients, donor kidneys less than 5 years of age,

recipients less than 2 years of age, patients previously transplanted, and cadaveric donors with a cold ischemia time of more than 24 hours. As mentioned before, recipient hydration and oxygen-carrying capacity must be optimal at the time of engraftment to ensure appropriate allograft perfusion. Engraftment of an organ can be a challenge in smaller patients and those who have undergone multiple prior transplants. Thus it requires ingenuity at times by the transplant surgeon to find appropriate vasculature and recipient lower urinary tract into which the donor renal artery, vein, and ureter can be implanted in order to prevent technical complications and graft loss.

VII. COMPLICATIONS AND GROWTH

A. Complications

Infections, both bacterial and viral, account for a majority of hospital admissions post transplantation. Viral infections especially due to herpes virus and cytomegalovirus can lead to systemic morbidity in this immunosuppressed population and often mimic acute rejection. Even more worrisome is Epstein-Barr exposure. The virus may cause posttransplant lymphoproliferative disease and lymphoma. The incidence of this disease has been reported at 1.6%. However, recent NAPRTCS data suggest the prevalence to be as high as 10%. Pneumocystis, an opportunistic infection, is preventable in most recipients by administering prophylactic sulfatrim in early posttransplant time period. Of course, the same antibiotics will minimize the risk of lower and upper urinary tract infections.

As opposed to infection, cardiovascular disease is a leading cause of death in posttransplant children. Hypertension often with decreased allograft function is very common in children after transplantation. NAPRTCS reports that at 5 years posttransplant, 71% versus 58% for

deceased versus live donor recipients require antihypertensive therapy. What is still unknown is if hypertension results in allograft damage or previous allograft damage causes hypertension. In any event, cardiovascular disease leads to almost 25% of the deaths in this population.

Urologic complications after renal transplantation represent 2.5% to 14% of complications. Extravesical ureteroneocystostomy (Fig. 24-1) is the most common technique used for ureteral anastomosis. Penna et al. (2017) recently reported favorable results on a series of 23 ureteroureterostomies (an end to side anastomosis between the transplant ureter and the native ureter). They advocate ureteroureterostomy in certain complex situations such as a small bladder due to anuria, a valve bladder, and a neurogenic augmented bladder.

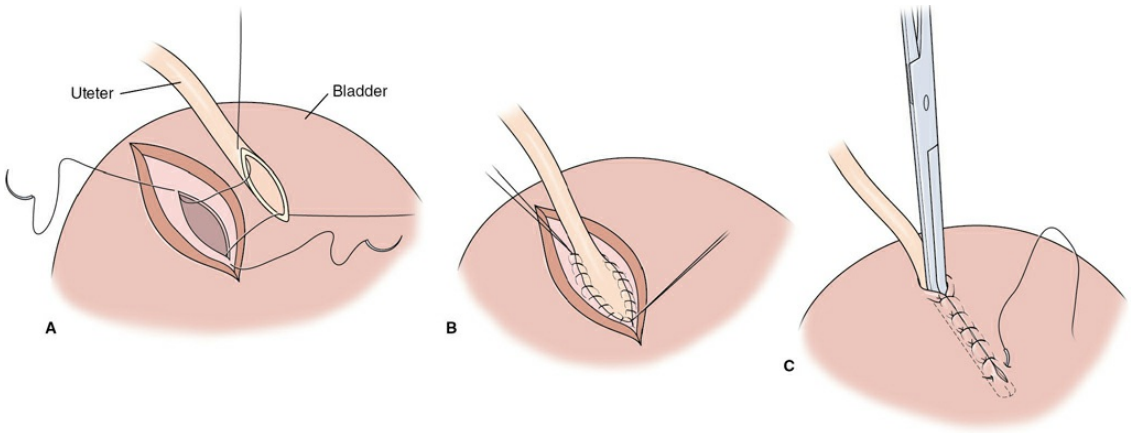

Fig. 24-1 A: Extravesical tunnel in the native bladder ready to accept the transplanted ureter. B: Native bladder/transplant ureter anastomosis. C: Closure of native bladder muscle to prevent reflux into the transplanted ureter.

B. Growth and Development

Growth failure continues to be a serious concern in children posttransplantation, where many children experience no improvement in growth. Subsequent growth correlates with patient age and amount of growth failure at the time of transplantation. Those children who undergo transplantation at a very early age, under 5 years,

will have the greatest degree of catch-up growth. However, these children never reach normal adult size. The cause of continued decreased growth after transplantation is due to several factors including an inherent abnormality of the growth hormone axis, steroid use, renal tubular acidosis, and failing allograft function. Although the use of alternate dosing of steroids can lead to improved growth, only 30% of patients are currently on this regiment. Finally, the use of recombinant growth hormone will lead to improvement in growth. In 1987, children receiving their initial transplant were an average of 2.43 standard deviations below average in height and 1.91 standard deviations below average in weight. This has improved over the past three decades to −1.16 in height and −0.60 in weight in 2013.

VIII. CONCLUSION

In reviewing the status of renal transplantation in children, we have seen that graft survival has improved tremendously over the past three decades. In spite of this, we still are plagued by complications such as infection and growth failure. The challenge in this new millennium will be to find waysto decrease the significant morbidity attendant with current immunosuppression and continue to discover new and superior medications. Until transplantation becomes a reality with a flat cadaveric donor pool, LRD will continue to provide an increasing majority of kidneys for human renal transplantation.

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25 Pediatric Urologic Oncology

Michael Ritchey

I. NEUROBLASTOMA

A. Epidemiology

Neuroblastoma is the most common extracranial solid tumor in children accounting for 8% to 10% of all childhood tumors. It is the most common malignant tumor in infancy and 89% of cases are diagnosed by 5 years of age.

B. Genetics

Neuroblastoma can be familial with an autosomal dominant mode of inheritance. Most cases are nonfamilial. Numerous chromosomal abnormalities occur in neuroblastoma in the form of chromosomal deletions, translocations, and cytogenetic evidence of gene amplification. Deletion of the short arm of chromosome 1 is found in 25% to 30% of cases and is an adverse prognostic factor. Amplification of the *MYCN* oncogene is seen in roughly 20% to 25% of primary tumors and is an adverse prognostic indicator.

C. Clinical Presentation

Most primary tumors arise within the abdomen and the majority present with abdominal pain or a palpable abdominal mass. Extrinsic compression of the bowel can produce symptoms. Metastasis is present in 70% of patients at diagnosis and can be responsible for a variety of symptoms. Some children present with rather unique paraneoplastic syndromes. Symptoms produced by catecholamine release may mimic those seen in pheochromocytoma.

D. **Diagnosis**

1. Increased levels of urinary metabolites of catecholamines, vanillylmandelic acid (VMA) and homovanillic acid (HVA) are found in 90% of patients.
2. Bone marrow involvement from metastatic tumor can produce anemia. Bone marrow biopsies and aspirates are performed to detect metastatic tumor.
3. Screening for metabolites of catecholamines has been employed widely in Japan. The goal is to detect disease at an earlier stage. Screening is successful in identification of neuroblastoma at a younger age, but there has been no decrease in the occurrence of neuroblastoma in older children and its subsequent mortality.
4. Plain radiographs may demonstrate a calcified abdominal or posterior mediastinal mass. Computed tomography (CT) and magnetic resonance imaging (MRI) provide more information about the local extent of the primary tumors and vascular involvement. MRI has advantages in the evaluation of intraspinal tumor extension. Imaging with both a radionuclide bone scan and metaiodobenzylguanidine (MIBG) scans are done for staging. MIBG scans use ^{131}I-MIBG which is taken up by the adrenergic secretory vesicles of the tumor cells in both primary and metastatic sites.

E. **Pathology and Staging**

1. Pathology
    a. Autopsy examination in infants has found neuroblastoma in situ in 1 out of 224 infants. Most of these small tumors regress spontaneously as the incidence of neuroblastoma is lower. It has been suggested that overt neuroblastomas can regress spontaneously. Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma display a histologic spectrum of

maturation and differentiation. Ganglioneuroma may arise de novo or result from maturation of preexisting neuroblastoma.

b. The Shimada classification is an age-linked histopathologic classification. It is used to stratify patients according to tumor prognosis categorizing the tumor as stroma poor or stroma rich. Patients with stroma-poor tumors with unfavorable histopathologic features have a very poor prognosis (less than 10% survival).

2. Prognostic variables
   a. Children aged 1 year or younger have an improved survival when compared with older children. This is attributed to more favorable biologic parameters in this age group.
   b. Site of origin has been correlated with survival. Nonadrenal primary tumors have a better prognosis.
   c. Stage of disease is one of the most important prognostic indicators. More advanced tumors, stages III and IV, require much more aggressive treatment.
   d. A special category is stage IV-S. These tumors primarily occur in infants. They often have small primaries associated with liver, skin, and bone marrow involvement without radiographic evidence of bony metastases. These patients have a good prognosis with many tumors undergoing spontaneous regression.
   e. n-myc amplification is associated with rapid tumor progression and a poor prognosis. n-myc amplification is found in 30% to 40% of advanced stage tumors. This is an adverse prognostic factor independent of the patient's age or stage of disease.
3. Stage of the disease is a significant prognostic variable. It is used to determine postoperative

adjuvant therapy.

International Neuroblastoma Staging System

Stage	Extent of Disease
1	Localized tumor with complete gross excision, with or without microscopic residual disease.
2A	Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically.
2B	Localized tumor with or without complete gross excision, with ipsilateral nonadherent lymph nodes positive for tumor.
3	Unresectable unilateral tumor infiltrating across the midline, with or without regional lymph node involvement; or localized unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral extension by infiltration (unresectable) or by lymph node involvement.
4	Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs.
4S	Localized primary tumor with dissemination limited to skin, liver, and/or bone marrow (less than 10% tumor) in infants younger than 1 year of age.

F. **Surgical Management**

1. Low-risk disease (stages I, II, IV-S): Children with low-stage disease have an excellent survival with surgical excision alone. Chemotherapy is indicated only in the event of recurrence unless the child has *MYCN* amplification and unfavorable histology. Resection of the primary is not mandatory for infants with IV-S disease. The vast majority of these infants have tumors with entirely favorable markers, explaining their good prognosis. However, a small fraction have adverse markers, and these children should be considered for a more aggressive treatment

with multimodal therapy.

2. High-risk disease (stages III, IV): There is some controversy regarding aggressive surgical resection at diagnosis. Many centers defer surgery until after completion of chemotherapy. The tumors are smaller and firmer, with less risk of rupture and hemorrhage following chemotherapy, resulting in a decreased rate of complications. Timing of surgery is generally 13 to 18 weeks after completion of therapy.

G. **Postoperative Treatment**

1. Chemotherapy: A variety of multi-agent treatments have been developed to treat high-risk patients. Despite marked treatment intensification, relapse continues to be a problem. The use of marrow ablative chemoradiotherapy followed by autologous marrow transplant has resulted in higher survival rates. Other modalities are being developed to target the tumor using biologic therapy.
2. Radiation therapy: Radiation therapy is primarily used for treatment for unresectable disease. Doses of external beam irradiation used have ranged between 15 Gy and 30 Gy, depending on the patient's age, location of the tumor, and extent of residual disease.

II. RHABDOMYOSARCOMA

A. **Epidemiology**

Rhabdomyosarcoma (RMS) accounts for 10% to 15% of all pediatric solid tumors with 20% of RMS arising in the genitourinary (GU) tract. The most common GU sites are prostate, bladder, and paratesticular. There is a bimodal age distribution with a peak incidence in the first 2 years of life and again at adolescence.

B. **Genetics**

The Li-Fraumeni syndrome results from germline mutations of the p53 tumor suppressor gene. Soft tissue sarcomas account for up to 20% of the tumors seen in these patients. Neurofibromatosis is an autosomal

dominant disorder. The incidence of RMS is estimated to be 10% in affected individuals. Other disorders with an increased risk for RMS are multiple endocrine neoplasia type 2A and Costello, Noonan, and basal cell nevus syndromes.

C. **Clinical Presentation**

Presentation will vary by tumor site. Bladder and prostate tumors often have a clinical presentation of urinary obstruction. This can be stranguria or urinary retention. Hematuria is common. Physical examination will often reveal a palpable abdominal mass.

Paratesticular rhabdomyosarcoma presents as a painless scrotal mass. It is usually detected at an earlier stage due to the superficial location.

Vaginal and vulvar rhabdomyosarcoma present with a vaginal mass and/or bleeding. Prolapse of the mass from the vaginal introitus can be quite striking. This is a typical finding with the sarcoma botryoides variant.

D. **Diagnosis**

CT or MRI is used to stage the extent of disease. It can be difficult to determine the site of origin of pelvic tumors. This is particularly true for distinguishing bladder and prostate tumors. In paratesticular rhabdomyosarcoma it is important to assess the lymph node status. Lymph nodes are the primary site of initial extension.

E. **Pathology and Staging**

1. Pathology: There are three main pathologic variants of rhabdomyosarcoma. Embryonal RMS is the most common subtype and accounts for most genitourinary tumors. This type can present as sarcoma botryoides, a polypoid variety that occurs in hollow organs or body cavities such as the bladder or vagina. The botryoides variants have excellent survival. The second most common type is alveolar and has a worse prognosis. Alveolar tumors can be categorized by the presence or absence of oncogenic fusion proteins produced by chromosomal translocations.

The majority of alveolar tumors are fusion-positive and have an inferior prognosis compared to fusion-negative alveolar tumors and embryonal RMS.

2. Staging: The Intergroup Rhabdomyosarcoma Study (IRS) Clinical Staging Classification is given below.

   Stage 1: Favorable site*, nonmetastatic
   Stage 2: Unfavorable site, small tumor, negative nodes, nonmetastatic
   Stage 3: Unfavorable site, big or positive nodes, nonmetastatic
   Stage 4: Any site, metastatic.
   In the genitourinary tract the testes, vagina, and uterus are more favorable than the prostate and bladder.

F. **Surgical Treatment**

The role or surgery will vary by site.

1. Paratesticular tumor: Initial intervention is radical orchiectomy. The tumor arises in the distal spermatic cord and may invade the testis or surrounding tissues. Retroperitoneal sampling is not recommended in children younger than 10 years of age. Children's Oncology Group (COG) recommends that children older than 10 years of age undergo ipsilateral retroperitoneal lymph node dissection prior to chemotherapy.
2. Bladder prostate: Surgical management of a bladder/prostate primary has become more conservative. Most patients receive chemotherapy and/or radiation prior to surgery. The goal is to shrink the tumor to allow bladder preservation. With intensification of treatment, 60% of the patients now retain a functional bladder with an overall survival of 85%. Tumors that are in the periphery of the bladder can be managed with partial cystectomy. If chemotherapy does not result in adequate shrinkage to allow partial resection, a radical cystectomy may be necessary.

G. **Postoperative Treatment**

Multimodality therapy is used in the treatment of rhabdomyosarcoma. The primary chemotherapy is vincristine, dactinomycin, and cyclophosphamide (VAC). For higher-risk tumors, more intensive regimens have

been utilized. Radiation therapy is given if the tumor fails to regress on chemotherapy. Survival rates vary by site.

1. Paratesticular: Survival of paratesticular RMS is excellent. This is due to several factors. Most of the tumors are stage I at diagnosis. More than 90% have embryonal histology. Overall 3-year survival in COG studies exceeds 90%.
2. Vagina or uterus: These tumors respond very well to preoperative therapy. Less than 15% require surgical resection. Radiation is needed to prevent local recurrence. Overall survival exceeds 90%.
3. Bladder or prostate: A major goal in treatment of patients with these tumors is bladder preservation. Overall 5-year survival is 84% with relapse-free survival of 75%. Most relapse occurs early with 60% being local failures alone and the remainder being distant failure with or without local relapse.

H. **Late Effects**

A primary concern is the late risk of bladder dysfunction in patients treated with pelvic irradiation. This can result in reduced decreased compliance leading to renal problems. Previously conducted clinical trials in patients with bladder/prostate RMS have not prospectively evaluated bladder function. While up to two-thirds of the bladders may be preserved, many will have abnormal bladder function.

Reproductive and sexual function can be impacted by multimodal treatment of RMS. Up to 80% of long-term female survivors will have endocrine or gynecologic dysfunction. Male survivors are also at increased risk for infertility and erectile dysfunction.

III. WILMS TUMOR

A. **Epidemiology**

Incidence of Wilms tumor in children aged 0 to 19 years is 6.3 cases per million. Median age at presentation is 3 years with 80% of the cases presenting under age 5.

Children with bilateral tumor present at a younger age.

B. **Genetics**

A number of recognizable syndromes are associated with an increased incidence of Wilms tumor. These are divided into overgrowth and non-overgrowth syndromes. The non-overgrowth syndromes include aniridia and the Denys–Drash syndrome. Aniridia is found in 1% of Wilms tumor patients. It is associated with WAGR syndrome (Wilms tumor, aniridia, genital anomalies, mental retardation). A deletion of chromosome 11 was first detected in these patients. Approximately 50% of the patients with the WAGR syndrome and chromosome 11 deletion will develop Wilms tumor.

Symptoms of overgrowth features include the Beckwith-Wiedemann syndrome (BWS). This is characterized by organomegaly such as nephromegaly and liver enlargement. Children with isolated hemihypertrophy also are at increased risk for Wilms tumor. The risk of Wilms tumor in BWS and hemihypertrophy is approximately 10%.

A number of genes have been identified that could be responsible for the development of Wilms tumor. WT-1 is located on chromosome 11p13 and is associated with patients with aniridia and Denys–Drash syndrome. WT-2 has been identified on imprinted region of chromosome 11p15. It has been linked to BWS. However, more than 80% of sporadic primary Wilms tumor may have loss of imprinting or loss of heterozygosity at 11p15.5. Somatic mutations of Wilms tumor gene on X chromosome (WTX) are identified in 20% to 30% of Wilms tumors.

Other chromosomal abnormalities have been found in Wilms tumor patients. The loss of heterozygosity (LOH) for chromosome 16q and 1p has been found to be associated with an adverse prognosis. TP53 (tumor protein 53) gene mutations are found in about 5% of Wilms tumors, associated with unfavorable (anaplastic) histology.

C. **Clinical Presentation**

A palpable abdominal mass is present in over 90% of children. Tumor rupture can occur leading to the signs and symptoms of an acute abdomen. Hematuria is a less common presentation but microscopic hematuria is common. Extension of the tumor into the venous drainage from the kidney can produce varicocele, ascites, and even congestive heart failure due to extension into the right atrium.

D. **Diagnosis**

Ultrasound will confirm a solid tumor and may identify the site of origin. Either CT or MRI is next performed in all children, but cannot distinguish Wilms tumor from other renal tumors of childhood. Diagnosis of extra renal extension of the tumor is important in staging. Imaging studies may suspect regional extension to surrounding organs but it is not that reliable. Imaging of the chest (CT or MRI) is needed to exclude pulmonary metastases. The contralateral kidney should be evaluated to exclude bilateral disease. Very few lesions are missed

Preoperative imaging should exclude intracaval extension. Ultrasound is useful in this regard. MRI is the study of choice if ultrasound is inconclusive.

Screening with serial renal ultrasounds has been recommended in children at high risk for development of Wilms tumor. It is recommended that screening be performed when a condition has a Wilms tumor incidence of greater than 5%. Ultrasound surveillance is performed from the time of diagnosis until 5 years of age, with a frequency of every 3 to 4 months. No studies to date have demonstrated that early detection has improved patient survival. Early detection can provide an opportunity for nephron sparing surgery, since these children are at an increased risk for bilateral disease. The smaller tumors found on screening studies are more amenable to renal sparing surgery. Screening of the contralateral kidney following nephrectomy for unilateral Wilms tumor is also

recommended.

E. **Pathology and Staging**

1. Pathology: Most tumors are categorized as favorable histology. Wilms tumor typically has three components: blastema, epithelial, and stroma. Anaplasia of the tumor is found in approximately 5% to 10% of children. It is associated with resistance to therapy. Complete excision of these tumors is mandatory. Other variants once thought to be Wilms tumor are now considered to be separate entities (see below).
2. Staging

   Stage extent of disease

   I Tumor limited to the kidney and completely excised. The renal capsule is intact and the tumor was not ruptured prior to removal. There is no residual tumor. No involvement of the renal sinus vessels.

   II Tumor extends through the perirenal capsule but is completely excised. Extrarenal vessels may contain tumor thrombus or be infiltrated by tumor but must be removed completely en bloc with nephrectomy specimen.

   III Residual non-hematogenous tumor confined to the abdomen: lymph node involvement, tumor spillage before or during surgery, tumor biopsied before resection, peritoneal implants, tumor beyond surgical margin either grossly or microscopically, or tumor not completely removed.

   IV Hematogenous metastases to lung, liver, bone, brain, etc.

   V Bilateral renal involvement at diagnosis.

F. **Surgical Treatment**

Surgical goals are complete removal of the tumor without rupture. The surgeon is responsible for evaluating extent of disease required for accurate staging of the tumor.

Sampling lymph nodes is imperative. Surgeons should look for evidence of extension to the other organs and ruptured tumor within the peritoneal cavity. Exploration of the contralateral kidney not indicated if imaging studies are negative for bilateral tumor.

The surgeon is responsible for removing the tumor intact. Tumor spillage results in a six-fold increase in local abdominal relapse. Local relapse is associated with a significant reduction in survival. Surgical complications remain common occurring in 11% of patients.

G. **Postoperative Treatment**

In North America most patients with Wilms tumor are treated with primary surgery followed by postoperative regimen therapy. In Europe and other countries, preoperative chemotherapy is the initial treatment. Results of these studies are reviewed.

1. Children's Oncology Group (COG): The overall survival for patients with favorable histology now exceeds 90%. The four-year overall survival in stage III patients is 90% and for stage IV 80%.

   Stage I disease favorable histology: if age is less than 24 months and tumor weight is less than 550g, observation only after initial surgery (surgery is not standard treatment and should only be done as part of clinical trial); if age is greater than 24 months or tumor is more than 550 g (1.2 lb), regimen EE-4A (vincristine and dactinomycin for 18 weeks) without radiation therapy.

   Stage I disease focal or diffuse anaplasia: regimen EE-4A and radiation therapy.

   Stage II disease favorable histology: regimen EE-4A without radiation therapy.

   Stage II–III disease focal anaplasia: regimen DD-4A (vincristine, dactinomycin, and doxorubicin for 24 weeks) followed by abdominal radiation therapy.

   Stage II–III disease diffuse anaplasia: regimen I (vincristine, doxorubicin, cyclophosphamide, and etoposide for 24 weeks) followed by abdominal radiation therapy.

   Stage III disease favorable histology: regimen DD-4A, then abdominal radiation therapy.

   Stage IV disease favorable histology and focal anaplasia: regimen DD-4A, then abdominal radiation therapy and radiation to sites of metastases. COG investigators have evaluted a response-based approach for management of pulmonary metastases. Children that have a complete response measured by chest CT avoid pulmonary

radiation.

Stage IV disease diffuse anaplasia: regimen I followed by abdominal radiation therapy and radiation to sites of metastases.

Children with anaplastic tumors continue to do poorly. More intensive chemotherapy regimens have been employed without any survival advantage. The four-year relapse-free survival remains poor.

A number of genetic and biologic factors have been identified that may be associated with adverse outcomes in patient with Wilms tumor. These include 16q and 1p loss, 1q gain, 11p15 methylation status, and WT1 mutation status. The cooperative groups are evaluating the feasibility of stratifying patients for therapy based on these findings.

2. International Society of Pediatric Oncology (SIOP): SIOP Wilms tumor protocols routinely utilize preoperative chemotherapy before surgery for most patients. Initial treatment is based on imaging without a biopsy. SIOP investigators use tumor stage, histology, tumor volume, and the response to preoperative chemotherapy for risk stratification. Preoperative chemotherapy leads to “downstaging” with only 40% of tumors being stage II or III. Tumors are categorized into low risk, intermediate risk and high risk. Low-risk tumors are those with tumor necrosis or cystic partially differentiated nephroblastoma. High-risk tumors include anaplastic tumors and blastemal predominant tumors as these are also associated with higher mortality. Tumor size less than 500 mL after chemotherapy is associated with improved survival in patients with intermediate-risk tumor histology.

   Chemotherapy consisting of dactinomycin and vincristine is given for 4 weeks followed by surgery. Patients with stage IV disease are given three drugs (doxorubicin is added) for 6 weeks. Patients with

pulmonary metastases who have complete response, with or without metastasectomy, have an improved survival. Only 14% of patients with lung metastases receive pulmonary radiation as part of their initial treatment.

3. Bilateral tumors: Five percent of patients present with bilateral tumors at diagnosis. These tumors often arise from precursor lesions known as nephrogenic rests. Preservation of renal tissue is necessary in this group of children who are at increased risk of renal failure. Preoperative chemotherapy is used in all patients with bilateral tumors. The recently completed COG study used an intensified chemotherapy at diagnosis. The hypothesis was that maximum tumor reduction could be obtained in a shorter interval leading to earlier surgical intervention. Investigators wanted to determine if this approach would lead to lower incidence of complete nephrectomy. Treatment after surgery followed the SIOP approach using post-chemotherapy histology to guide the chemotherapy regimen and duration.

H. **Late Effects of Treatment**

1. Numerous organ systems are subject to late sequelae of anticancer therapy. Early reports found that irradiation could result in scoliosis. The radiation dose was decreased and the radiation portals were changed. Musculoskeletal problems are now much less common.
2. Gonadal radiation can produce infertility in both boys and girls. A 12% incidence of ovarian failure has been noted after abdominal radiation therapy. This abdominal radiation can also lead to adverse pregnancy outcomes.
3. Doxorubicin is associated with an increased risk of congestive heart failure. Cardiomyopathy can develop many years after treatment. The incidence of congestive heart failure is 4.4% among Wilms tumor

patients receiving doxorubicin as their initial chemotherapy regimen.

4. An increased risk of renal failure has been found in patients with bilateral tumors. Patients with Wilms tumor in association with aniridia, and genitourinary anomalies also have an increased risk of renal failure, occurring more than 10 years after initial treatment. Children with Denys–Drash syndrome have an increased risk of renal failure due to coexistent glomerulopathy.

IV. OTHER RENAL TUMORS

A. **Congenital Mesoblastic Nephroma (CMN)**

CMN is the most common renal tumor in infants. These tumors are predominantly composed of bundles of spindle cells resembling smooth muscle cells. Most of these patients are cured with nephrectomy alone. Some tumors with increased cellularity have been noted to develop local recurrence. The risk is greatest in children under 3 months of age.

B. **Cystic Partially Differentiated Nephroblastoma (CPDN)**

The majority of these tumors occur in the first year of life. Some authorities consider multilocular cystic nephroma to be the same entity. They are indistinguishable radiographically. The CT shows cysts of varying size sometimes with a prominent septa. Surgery is curative in almost all patients if the tumor is completely removed. For those with incomplete resection, postoperative dactinomycin and vincristine are administered. Partial nephrectomy can be performed if the tumor is confined to the pole of the kidney.

C. **Clear Cell Sarcoma of the Kidney (CCSK)**

CCSK accounts for 3% of renal tumors. The age at diagnosis is similar to nephroblastoma. Prognosis is improved in those with lower stage. Doxorubicin has greatly improved survival of these children. They all

require radiation therapy. Patients with stage I tumor have a 98% survival rate. Late recurrences can occur. These tumors are unique in that they are prone to bone and brain metastasis.

D. **Rhabdoid Tumor of the Kidney (RTK)**

RTK is the most aggressive and lethal renal tumor. It accounts for 2% of renal tumors. It typically occurs at a very young age with a median age diagnosis of 16 months. It is very unresponsive to chemotherapy and most patients with metastatic disease do not survive.

E. **Renal Cell Carcinoma (RCC)**

RCC is the most common renal tumor in the second decade of life. Imaging studies cannot differentiate RCC from other solid renal tumors. There is a higher incidence of papillary RCC in children. These tumors, typically seen in adolescence or young adults, are genetically unique in that they have chromosome translocations involving a common breakpoint in the TFE gene located at Xp11.2. Another type of RCC more often seen in children is renal medullary carcinoma found in patients with sickle cell hemoglobinopathy. The median age at presentation is 13 years, but can be found in much younger children. It is a highly lethal tumor.

Complete tumor resection is the most important determinant of outcome. Patients with stage I tumors usually survive. Regional lymph node involvement does not portend the same poor prognosis as adult renal cell carcinoma. No studies have been conducted to identify effective adjuvant treatment for higher stage patients.

F. **Angiomyolipoma (AML)**

Angiomyolipoma will develop in 80% of patients with tuberous sclerosis complex (TSC). The incidence of AML increases with age in these patients. Annual ultrasounds are recommended to detect growth of tumors. Some lesions are fat-poor and differentiation from other renal tumors, for example RCC that can occur in these children, on imaging studies can be difficult. In some cases biopsy

of the lesion may be needed to confirm diagnosis of AML before proceeding with treatment. The risk of bleeding increases with lesions greater than 4 cm in diameter. Selective angiographic embolization has been used for treatment. More recently, mTOR inhibitors have shown promise as a new type of therapy for reducing the size of TSC-associated angiomyolipomas and represent the first systemic therapeutic approach to treat the underlying cause of TSC (i.e., targeting unregulated mTOR activation).

V. TESTICULAR TUMORS

A. Epidemiology

Testicular tumors represent 1% of all solid pediatric tumors. Benign lesions occur more commonly in children than adults. Recent reports have noted benign testicular lesions such as teratoma occur more often than germ cell malignancy. The incidence of childhood testicular tumor peaks at age 2 years, but rises again after puberty.

B. Pathogenesis and Genetics

There is a known increased risk of germ cell tumors (GCT) in patients with a history of cryptorchidism. Patients with disorders of sexual differentiation are also at increased risk, particularly those with Y chromosomal material in their karyotype. Intratubular germ cell neoplasia (IGCN) has been found with increased incidence in adults with a history of undescended testes. IGCN is thought to be a precursor lesion to the development of GCT. A variety of chromosomal abnormalities have been found in both adolescent and adult germ cell tumors. These include deletions of 1p, loss of 6q, and abnormalities of 2, 3p, and 12p. The latter may have a role in development of IGCN, but none have been found to have prognostic significance.

C. Clinical Presentation

Painless testicular mass is the most common clinical finding. Unfortunately, many patients can be

misdiagnosed with other benign conditions such as epididymitis, hydrocele, or hernia. Testicular ultrasound is invaluable in assessing scrotal pathology. Ultrasound is particularly helpful to identify cystic components of testicular teratoma and also epidermoid cysts. The latter is described as having an “onion skin” appearance. Recognition of these lesions preoperatively can provide for a testis-sparing procedure.

D. **Diagnosis**

CT of the retroperitoneum and chest are necessary to exclude metastatic lesions in germ cell tumors. Most retroperitoneal lymph node metastasis can be identified but 15% to 20% are missed.

Tumor markers are important in germ cell tumors. α-Fetoprotein (AFP) is produced by tumors that contain yolk sac elements. Assessment of AFP after removal of tumor is essential. Persistently high levels reflect metastatic disease. The exception is that in infants, normal adult levels are not reached. β-*hCG* is produced by embryonal and mixed germ cell tumors. It is not commonly elevated in prepubertal patients.

E. **Pathology and Staging**

1. Staging

St.ge	Extent of disease
I	Tumor is limited to the testis. Tumor markers are negative after appropriate half-life decline.
II	Microscopic residual disease is present in the scrotum or spermatic cord. Tumor markers remain elevated after appropriate half-life interval. Tumor rupture or scrotal biopsy prior to complete orchiectomy.
III	Retroperitoneal lymph node metastases.
IV	Distant metastases.

2. Pathology
    1. Teratoma is the most common germ cell tumor in prepubertal children. The tumor may have elements from more than one germ cell layer.

The microscopic appearance varies with the degree of maturation and the amount of tissue from each germ cell layer.

2. Yolk sac tumor is also known as endodermal sinus tumor. A characteristic finding in yolk sac tumors is Schiller-Duval bodies. Special staining will demonstrate the presence of α-fetoprotein.
3. Leydig cell tumors, Sertoli cell tumors, and granulosa cell tumors have a common embryologic origin. The pathologic feature of Leydig cell tumor is Reinke's crystal present in 40% of the tumors.
4. Gonadoblastomas are the most common tumors found in patients with disorders of sex development. The germ cell component of gonadoblastoma is prone to malignant degeneration. The tumors occur in dysplastic or streak gonads.

F. **Surgical Treatment**

Malignant tumors are managed by radical inguinal orchiectomy. Scrotal approach to a testicular mass is avoided. This leads to an increase in stage of the tumor and requires more intensive therapy. Benign tumors such as teratoma and epidermoid cysts are amenable to a testis-sparing approach in some cases. With complete excision of the lesion, no cases of recurrence have been noted.

G. **Postoperative Treatment**

1. Mature teratoma: Radical orchiectomy or partial orchiectomy is curative in prepubertal patients. Assessment of retroperitoneal lymph nodes is mandatory after puberty. Immature teratoma is less common. It occurs more often in the ovary than the testis. Recurrence of an immature teratoma may occur in patients with elevated AFP or evidence of yolk sac tumor in the specimen.
2. Epidermoid cyst: Epidermoid cysts account for 15% of prepubertal testis lesions. They can be managed by

testis-sparing surgery. These patients do not require active surveillance after surgery.

3. Yolk sac tumors: Initial treatment for yolk sac tumors is radical orchiectomy. This is curative in most children. Clinical stage I patients do not receive adjuvant therapy after radical orchiectomy. Careful surveillance is performed. If elevation of AFP is noted, chemotherapy is begun.

   Patients with stage II to stage IV tumors will be treated with three cycles of compressed PEB (cisplatin, etoposide, and bleomycin). If a patient has only a partial response then six cycles of chemotherapy will be given. Persistent retroperitoneal masses after chemotherapy are uncommon. Survival for all patients approaches 100%.

4. Gonadal stromal tumors: Inguinal orchiectomy is curative for Leydig cell tumors in prepubertal children. Sertoli cell tumors occur in children as young as 4 months of age. Some of these tumors are hormonally active. Children younger than 5 years of age are usually managed with orchiectomy alone. However, those with adverse histologic features, for example vascular invasion or increased mitotic activity, and children greater than 5 years of age require more extensive staging.

VI. OTHER BLADDER TUMORS

A. Nephrogenic Adenoma

Nephrogenic adenoma is a benign tumor that can occur in both children and adults. It is typically seen in patients with recurrent infections, radiation, prior bladder surgeries, and other forms of bladder injury. It has also been reported after renal transplantation in immunosuppressed patients. It is felt to be a metaplastic lesion. Endoscopically the lesions are typically small and would appear consistent with papillary transitional cell

carcinoma. A biopsy is necessary to make the initial diagnosis. Treatment consists of excision and fulguration. These tumors can recur and surveillance is required although at less frequent intervals than for transitional cell carcinoma of the bladder.

B. **Transitional Cell Carcinoma**

Transitional cell carcinoma of the bladder rarely occurs in children and adolescents. Most cases are found in isolated case reports. These tumors can also occur as a second malignant neoplasm after prior treatment with cyclophosphamide. Most lesions are superficial and low grade. Endoscopic resection is the primary treatment and intravesical therapy is not routinely employed. There is some suggestion that there is a lower risk for recurrence for transitional cell carcinoma that occurs in younger children. Many authors recommend monitoring with bladder ultrasound to detect recurrences.

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* Paratesticular vulva–vagina–uterus

26 Robotic and Laparoscopic Surgery in Pediatric Urology

Eric A. Kurzrock

I. Introduction

Since the last edition of the *Handbook of Pediatric Urology*, advancements in robotic-assisted surgery have led to an exponential increase in pediatric laparoscopic surgery particularly for upper tract reconstruction. The laparoscopic approach has the advantages of smaller incisions, less pain, shorter hospitalization, and reduced convalescence for adults undergoing abdominal surgery. Infants and children benefit also but the advantages over open surgery probably decrease with the size of the patient. Since a child's bladder and kidneys are much closer to the surface and smaller, they can be repaired or removed through small (2- to 5-cm) open incisions with less division of muscle. Yet, the combination of excellent exposure and vision via the laparoscope with improved fine motor control via the robot has challenged the superiority of many pediatric open urologic procedures.

II. PHYSIOLOGY

Having the abdomen insufflated with CO_2 under pressure creates unique physiologic changes distinct from open surgery. Laparoscopic surgery is generally performed at pressures between 10 mm Hg and 15 mm Hg, which cause decreases in diaphragmatic movement and pulmonary

capacity. The absorption of CO_2 (hypercarbia) with the pressure can lead to cardiopulmonary changes that the surgeon and anesthesiologist have to follow and prepare to compensate. These include decreased cardiac output, increased heart rate, lower urine output, and increased intracranial pressure. Long-duration surgeries and/or cardiopulmonary comorbidities may prevent some patients from having laparoscopic surgery.

III. Instrumentation and Technique

Laparoscopic telescopes are available in 2- to 12-mm sizes. The initial port placement can be done blindly with a Veress needle, through an open incision, or with trocars that allow direct vision. It is very important to ensure an empty bladder prior to placing the first port. One to four more ports are then placed under direct laparoscopic vision. Most pediatric procedures are performed with 3.5- or 5-mm working instruments. A full array of instruments is available including dissectors, graspers, needle-drivers, cautery, and suction devices. Coagulation and division of tissue can be performed with similar instruments as open surgery such as scissors, mono- or bipolar cautery, and ultrasonic devices. Ligation of vessels and tissue can be accomplished with suture, clips, and staplers. Most surgeons prefer the robot if there is a reconstructive component to the surgery with suturing. Morcellators and bags may be used for specimen removal.

The laparoscope provides magnification, but the instruments and port angles often limit the surgeon’s dexterity and movement. Robotics can obviate these problems. As mentioned previously, advantages of the laparoscopic approach decrease inversely with patient size. The working space in small children and infants limits distance between ports and movement of instruments. Single-site (port) surgery

that allows the use of up to three instruments through one incision is gaining popularity in adults but will probably have limited utility in small children.

Most laparoscopic procedures are performed within the peritoneum. Some surgeons employ a retroperitoneal approach for kidney procedures. Operating within the peritoneal space has the advantage of more working space, but there is a risk of injuring bowel or the theoretical risk of inducing bowel adhesions. Retroperitoneoscopy is hindered by a smaller working area, but the renal hilum is easier to expose without bowel, liver, or spleen obstructing the view.

IV. Diagnostic Uses

A. **Inguinal Hernia**

A metachronous, contralateral hernia will develop in 5% to 10% of children. Age, sex, and side affect the risk. Prior to laparoscopy, contralateral, open inguinal exploration was the standard for young children. Laparoscopy obviates a contralateral incision in most children. During hernia repair, a 70°- or 120°-telescope is passed through the ipsilateral hernia sac. The contralateral, internal ring is easily visualized. If significantly patent, contralateral hernia repair is performed. The cost/benefit of this practice has been questioned and argues for limiting use of contralateral inspection to premature infants.

B. **Non-palpable Undescended Testis**

There is no imaging modality that is 100% sensitive in identifying an intra-abdominal testis. Laparoscopy can easily determine the presence and location of a testicle. Findings include the following.

1. Intra-abdominal testis
    a. Usually near the internal ring.
    Occasionally the testis is in the pelvis or near the kidney.

2. Vas deferens and gonadal vessels pass through internal ring
    a. An open ring suggests an inguinal testis.
    b. Atretic vessels and a closed ring suggest an atrophic testis in the scrotum or inguinal canal.
3. Gonadal vessels fade away before entering the internal ring
    a. If a blind-ending vessel is absolutely evident, inguinal exploration is considered unnecessary by many surgeons.

C. **Disorders of Sexual Development**

Laparoscopy allows delineation of internal genital structures and possible biopsy, and removal of internal gonads at risk for cancer.

V. Therapeutic Uses

A. **Abdominal Testis**

For the intra-abdominal testis, outcomes after laparoscopic orchiopexy such as testicular scrotal position and viability are comparable to open techniques. Laparoscopy is particularly advantageous for older boys and those with high, abdominal testicles. For a two-stage Fowler-Stephens orchiopexy, ligation of the gonadal artery during the first stage is simplified by laparoscopy. The second stage can be completed using either open or laparoscopic technique.

B. **Pyeloplasty**

After orchiopexy, pyeloplasty is the most common pediatric laparoscopic procedure. Robotic assistance is now used at most centers (Fig. 26-1). Long-term relief of obstruction is equitable between open and robotic approaches. More contemporary analysis has shown that shorter length of stay afforded by robotic pyeloplasty is no longer limited to older children and many centers are now treating infants and small children.

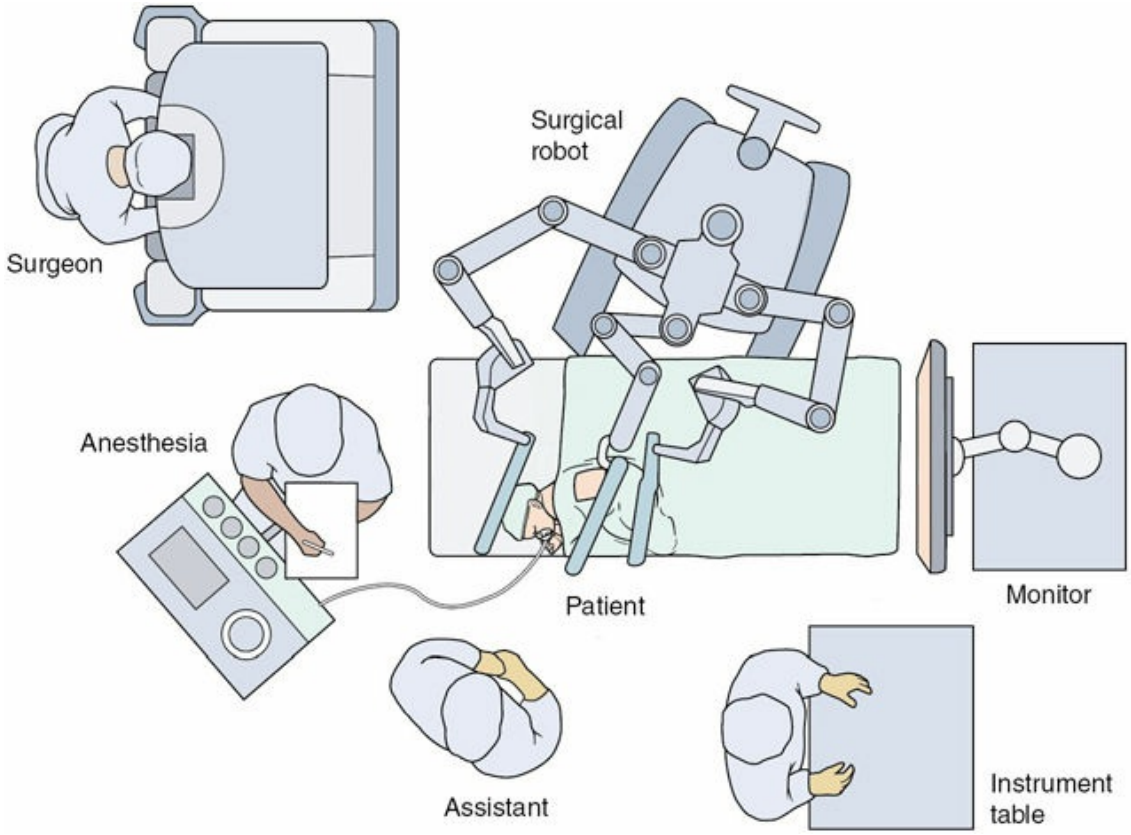

Fig. 26-1 Robotic pyeloplasty set-up with patient and surgeon's counsel.

C. **Nephrectomy and Nephroureterectomy**
   1. Indications
      a. Nonfunctional kidney secondary to the following.
         (1) Cystic disease
         (2) Reflux nephropathy
         (3) Hydronephrosis
      b. Donor transplant
      c. Pretransplant nephrectomy
   2. Relative contraindications
      a. Tumor
      b. Trauma
      c. Infection

D. **Partial Nephrectomy**
   1. Indications
      a. Duplex kidney
         (1) Poorly functioning upper pole associated

with ureterocele or ectopic ureter (Fig. 26-2).

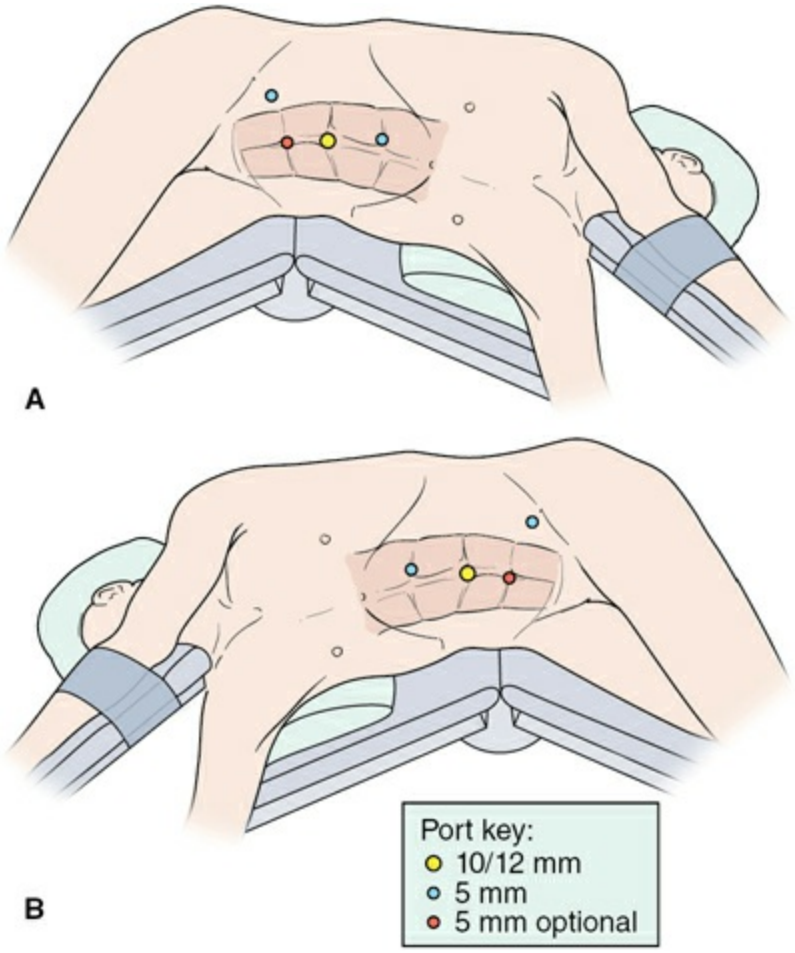

Fig. 26-2 Laparoscopic upper pole partial nephrectomy surgical set-up.

(2) Poorly functioning lower pole associated with reflux.

E. **Ureteral Reimplantation**

When done laparoscopically, the most popular approach is extravesical Lich-Gregoir with robotic assistance. Few centers utilize a laparoscopic approach for bladder surgery since endoscopic alternatives have become popular for low-grade reflux, and ureters with high-grade reflux are difficult to treat extravesically.

F. **Other Laparoscopic (or Laparoscopic-Assisted) Procedures**

1. Ureteroureterostomy
2. Appendicocecostomy
3. Urachal excision
4. Enterocystoplasty
5. Continent urinary diversion

Recommended Reading

Chan Y, Sturm R, Durbin-Johnson B, Kurzrock EA. Outcomes after pediatric open, laparoscopic and robotic pyeloplasty at academic institutions. *J Pediatr Urol* epub ahead of print: http://www.sciencedirect.com/science/article/pii/S1477513116303047.

Docimo SG, Peters CA. Pediatric endourology and laparoscopy. In: Walsh PC, Retik AB, Vaughan ED, Wein AJ, eds. *Campbell-Walsh Urology, 11th ed.* Philadelphia, PA: Elsevier; 2016:2963.

27 Anesthesia for Pediatric Urologic Procedures

Melissa A. Ehlers and Igor Galay

I. INTRODUCTION

Surgery is a stressful event for everyone, and even more so for children who may not understand the reason for their surgery. A well-designed anesthetic plan is necessary to allow for safe and effective surgery and also to reduce the amount of stress children and their families face at the time of surgery.

The goals of the anesthesiologist are given below.

- Reduce anxiety of patient and parents.
- Ensure patient comfort and safety during and after the procedure.
- Provide optimal surgical conditions.
- Reduce the negative impact of the stress response to surgery.
- Facilitate early recovery.

II. PREOPERATIVE PREPARATION

A. Allay Fears Early

Preparation for school-age children should start 5 to 7 days in advance to be effective. Besides discussing the risks and benefits of a certain procedure with the parents (and the patient if age is appropriate), it is usually helpful to describe to the family what to expect when they arrive at the hospital. Printed materials with instructions and a description of the perioperative process are frequently given to parents in the surgeon's office (see an example of

our brochure which attempts to explain some of the common questions asked about anesthesia in a child; Fig. 27-1). Some hospitals give tours for prospective patients and their families where they can see the check-in area, surgical holding area, recovery room, and pediatric ward or intensive care unit (ICU) if admission is planned. Other hospitals may have online videos to view for those patients who live far away or have difficulty getting to the hospital for a tour (see our example at http://www.amc.edu/patient/services/anesthesiology/videos/preop. Extensive preparation may be less helpful in children younger than 3 years or those who were hospitalized previously.

Your Child
& Anesthesia
The Department of Anesthesiology welcomes you and your child to The Children's Hospital at Albany Medical Center.
Surgery can be a very anxious time for both you and your child. This pamphlet is designed to answer some of your questions associated with surgery and anesthesia.
The Children's Hospital
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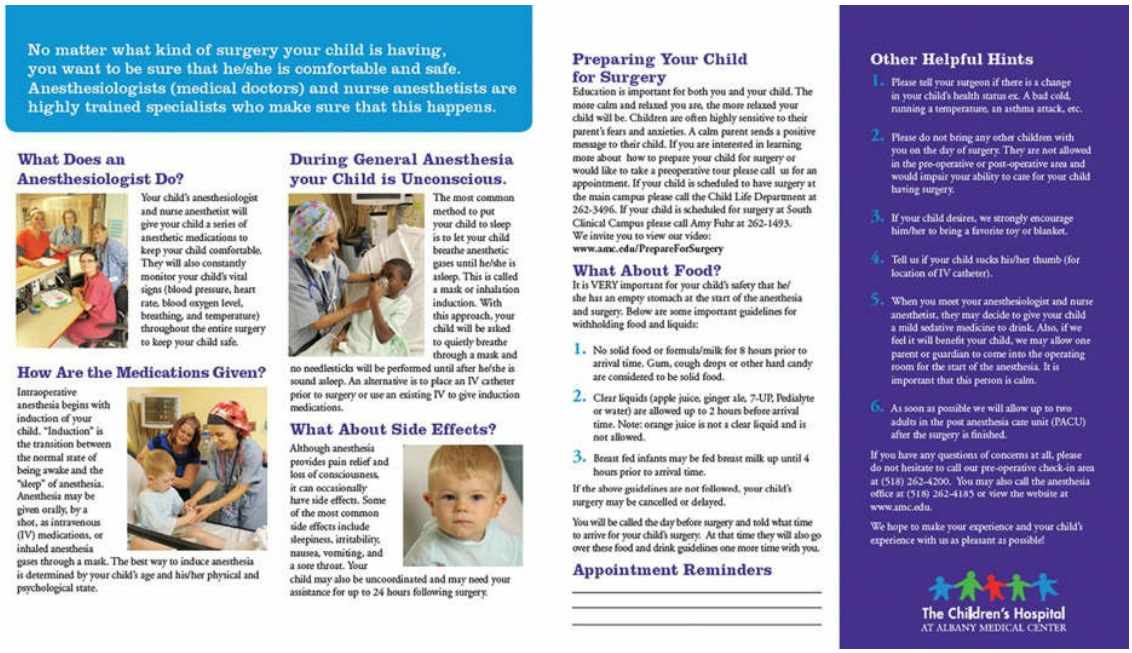

No matter what kind of surgery your child is having, you want to be sure that he/she is comfortable and safe. Anesthesiologists (medical doctors) and nurse anesthetists are highly trained specialists who make sure that this happens.

What Does an Anesthesiologist Do?

Your child's anesthesiologist and nurse anesthetist will give your child a series of anesthetic medications to keep your child comfortable. They will also constantly monitor your child's vital signs (blood pressure, heart rate, blood oxygen level, breathing, and temperature) throughout the entire surgery to keep your child safe.

How Are the Medications Given?

Intraoperative anesthesia begins with induction of your child. "Induction" is the transition between the normal state of being awake and the "sleep" of anesthesia. Anesthesia may be given orally, by a shot, as intravenous (IV) medications, or inhaled anesthesia gases through a mask. The best way to induce anesthesia is determined by your child's age and his/her physical and psychological state.

During General Anesthesia your Child is Unconscious.

The most common method to put your child to sleep is to let your child breathe anesthetic gases until he/she is asleep. This is called a mask or inhalation induction. With this approach, your child will be asked to quietly breathe through a mask and no needlesticks will be performed until after he/she is sound asleep. An alternative is to place an IV catheter prior to surgery or use an existing IV to give induction medications.

What About Side Effects?

Although anesthesia provides pain relief and loss of consciousness, it can occasionally have side effects. Some of the most common side effects include sleepiness, irritability, nausea, vomiting, and a sore throat. Your child may also be uncoordinated and may need your assistance for up to 24 hours following surgery.

Preparing Your Child for Surgery

Education is important for both you and your child. The more calm and relaxed you are, the more relaxed your child will be. Children are often highly sensitive to their parent's fears and anxieties. A calm parent sends a positive message to their child. If you are interested in learning more about how to prepare your child for surgery or would like to take a preoperative tour please call us for an appointment. If your child is scheduled to have surgery at the main campus please call the Child Life Department at 262-3496. If your child is scheduled for surgery at South Clinical Campus please call Amy Fuhr at 262-1493. We invite you to view our video: **www.amc.edu/PrepareForSurgery**

What About Food?

It is VERY important for your child's safety that he/she has an empty stomach at the start of the anesthesia and surgery. Below are some important guidelines for withholding food and liquids:

1. No solid food or formula/milk for 8 hours prior to arrival time. Gum, cough drops or other hard candy are considered to be solid food.
2. Clear liquids (apple juice, ginger ale, 7-UP, Pedialyte or water) are allowed up to 2 hours before arrival time. Note: orange juice is not a clear liquid and is not allowed.
3. Breast fed infants may be fed breast milk up until 4 hours prior to arrival time.

If the above guidelines are not followed, your child's surgery may be cancelled or delayed.

You will be called the day before surgery and told what time to arrive for your child's surgery. At that time they will also go over these food and drink guidelines one more time with you.

Appointment Reminders

Other Helpful Hints

1. Please tell your surgeon if there is a change in your child's health status ex. A bad cold, running a temperature, an asthma attack, etc.
2. Please do not bring any other children with you on the day of surgery. They are not allowed in the pre-operative or post-operative area and would impair your ability to care for your child having surgery.
3. If your child desires, we strongly encourage him/her to bring a favorite toy or blanket.
4. Tell us if your child sucks his/her thumb (for location of IV catheter).
5. When you meet your anesthesiologist and nurse anesthetist, they may decide to give your child a mild sedative medicine to drink. Also, if we feel it will benefit your child, we may allow one parent or guardian to come into the operating room for the start of the anesthesia. It is important that this person is calm.
6. As soon as possible we will allow up to two adults in the post anesthesia care unit (PACU) after the surgery is finished.

If you have any questions of concerns at all, please do not hesitate to call our pre-operative check-in area at (518) 262-4200. You may also call the anesthesia office at (518) 262-4185 or view the website at www.amc.edu.

We hope to make your experience and your child's experience with us as pleasant as possible!

The Children's Hospital
AT ALBANY MEDICAL CENTER

FIG. 27- 1

B. **Who Needs to Be Prescreened?**

Not every child has to be evaluated by an anesthesiologist in a formal prescreening clinic. For the majority of healthy patients, a phone interview several days before surgery may be sufficient. Patients with systemic diseases, syndromes, and/or a history of problems with anesthesia should be referred to a more formal prescreening process. The goal of preoperative evaluation is to collect all necessary information before the patient arrives at the hospital and to thereby avoid surprises and possible delays or cancellations on the day of surgery.

Upper respiratory infection is frequent in young children scheduled for surgery in a cold season. It is associated with a higher incidenceof respiratory complications (laryngospasm, bronchospasm) after general anesthesia. If the child is febrile, has a productive cough, or lower airway involvement (active wheezing or rales that do not clear with coughing), then it is prudent to delay surgery until the illness is over, ideally for six weeks.

C. **ASA Classification of Physical Status (by the**

American Society of Anesthesiologists)

1. Class 1: There is no organic, physiologic, biochemical, or psychiatric disturbance. The pathologic process for which the operation is to be performed is localized and is not a systemic disturbance.
2. Class 2: Mild to moderate systemic disturbance caused either by the condition to be treated surgically or by other pathophysiologic processes.
3. Class 3: Severe systemic disturbance or disease from whatever cause, even though it may not be possible to define the degree of disability with finality.
4. Class 4: Indicative of the subject with a severe systemic disorder already life threatening, not always correctable by the operative procedure.
5. Class 5: The moribund subject who has little chance of survival but is submitted to an operation in desperation.

D. **Common Syndromes with Specific Implications for Anesthetic Management (Not Meant to Be an All-Inclusive List)**

1. Beckwith-Wiedemann syndrome: Difficult airway, neonatal hypoglycemia.
2. Down syndrome (trisomy 21): Difficult airway, sleep apnea, atlantoaxial instability, congenital heart disease.
3. Goldenhar syndrome: Difficult airway, congenital heart disease.
4. Hemolytic uremic syndrome (HUS): Renal failure, hepatic dysfunction, seizures, coagulopathy.
5. Pierre Robin syndrome: Difficult airway, congenital heart disease.
6. Prune belly syndrome: Difficult airway, congenital heart disease.
7. VATER (or VACTERL) syndrome: Congenital heart disease, gastrointestinal (GI) atresias, tracheoesophageal fistula, renal issues.

E. **NPO Guidelines**

Fasting prior to surgery is necessary to ensure an empty stomach and to minimize the risk of aspiration during induction of anesthesia when protective airway reflexes are lost.

The American Society of Anesthesiologists recommends the following fasting times for healthy patients without delayed gastric emptying.

- 2 hours for clear liquids
- 4 hours for breast milk
- 6 hours for light meal or nonhuman milk. High-fat foods may prolong gastric emptying time

In case of emergent surgery, anesthesiologists may use some techniques to minimize the chance of aspiration such as suctioning of the stomach and rapid sequence induction. The risk of aspiration should however be weighed against the risk of delaying the surgery.

III. DAY OF SURGERY

A. **Parental Reassurance and Preparation**

This is very important since calm parents keep the young child from being unduly alarmed about their trip to the hospital and likewise provide a model for the older child or adolescent who is undergoing an operation.

B. **Premedication**

Depending on the child's level of anxiety and anticipated cooperation, an oral premedication is frequently given. Midazolam is the most frequently used drug as it has a relatively fast onset, ease of administration (works as well orally as it does intranasal or per rectum), and low side effect profile. Studies have shown that children who receive a premedication show less anxiety at induction, are more cooperative, and have fewer regressive behaviors postoperatively (e.g., bedwetting, temper tantrums), all of which contribute to a significant decrease in parental anxiety as well.

C. **Parents in the Operating Room (OR)**

There is general agreement about the desirability of parents staying with their child during hospitalization. Parental presence during the induction of anesthesia remains controversial. A majority of pediatric hospitals allow it. However, it is less effective in reducing anxiety than premedication with midazolam. On the other hand, it may be effective when a calm parent accompanies and distracts an anxious child on the way to the OR. Parental satisfaction with the perioperative process has been shown to be improved if they are allowed to be with their child during induction of anesthesia.

D. **Mode of Anesthesia**

The vast majority of pediatric urologic procedures are performed under general anesthesia (GA). Most younger children undergo an inhalational induction of anesthesia followed by placement of the IV and airway management.

Occasionally spinal anesthesia may be utilized as the sole anesthetic for infants (usually up to around 6 months old) or in the mature adolescent. When a spinal anesthetic is used, it is important to remember not to allow anyone to lift the legs (usually this occurs for electrocautery grounding pad placement) for at least 10 minutes after the spinal is in place as this may allow the local anesthetic to migrate so far cranially as to cause respiratory compromise or even a total spinal.

E. **Safety of General Anesthesia (GA) in Children**

There has been a great historical success in improving the safety of GA in children. Anesthesia-related mortality decreased from 16 per 10,000 in the 1950s to less than 0.3 per 10,000 in the 1990s. Neonates and infants younger than 1 year of age appear to have a higher risk of adverse respiratory and cardiac events compared to older children.

Very young patients (less than 60 weeks gestational age, especially if born at less than 36 weeks) may need to be admitted to the hospital for respiratory monitoring even after minor procedures since they are at risk for

postoperative apnea. It is important for a surgeon to know the hospital policy regarding this issue.

F. **General Anesthesia and the Developing Brain**

There has been much recent concern about the safety of anesthetic drugs in children. Multiple animal studies show long-term injury to the developing brain of neonatal animals exposed to various anesthetics. Some but not all studies suggest similar problems could occur in infants and toddlers. On December 14, 2016 the Food and Drug Administration (FDA) released a statement that said in part, "We are issuing a Drug Safety Communication to inform health care providers, parents and caregivers of children younger than three years, and pregnant women in their third trimester, that the repeated or lengthy (more than three hours) use of general anesthetic and sedation drugs may adversely affect children's developing brains." (See http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements for the full statement.) Obviously, as this issue becomes more and more prevalent in the news, parents are going to have many questions for their anesthesia providers as well as the physician ordering the procedure that requires anesthesia. Unfortunately, clinical science is lagging far behind and for every study that claims to show a possible harm from anesthesia, there seems to be another study that shows no difference. In summary, it is not yet possible to know whether the use of anesthetic agents poses a risk, and if so, whether the risk is large enough to outweigh the benefit of the planned procedure, but this should be considered carefully when deciding at what age elective surgery will be planned. For up-to-date information on the status of this very active debate, please visit http://smarttots.org/.

IV. PAIN CONTROL

Numerous studies have found that children's pain in general is undertreated, so it is very important to recognize and address

this problem. Self-reporting is used for assessment in older patients (see Fig. 27-2 for a commonly used tool) while a behavioral/observational scale (face, legs, activity, cry, consolability [FLACC]) is used for nonverbal children. Pain, however, should be assessed in the context of other sources of distress in a child (hunger, nausea, separation from parents, etc.).

A. Regional anesthesia (neural blockade with local anesthetics) is rarely used as a sole anesthetic in children but often is utilized as an adjunct to general anesthesia. The benefits include improved analgesia, suppression of the stress response, reduction in volatile agents, reduced need for ventilatory support after major surgeries, and a reduced need for opioid medications for postop pain control. Most nerve blocks are placed while the child is anesthetized in the operating room. A recent review of more than 50,000 nerve blocks has shown that serious complications are very rare.
    1. Neuraxial blocks
        a. Spinal: Injection of local anesthetic in the subarachnoid space provides a very dense nerve block for perineal and lower abdominal surgery. Duration of the blockade is limited to less than 2 hours, which limits its utility for postoperative pain control. In infants, this may, however, enable completion of a shorter procedure (e.g., hernia repair or circumcision) without general anesthesia.

            Epidural

            Caudal epidural: This is probably the most common type of regional anesthesia performed in pediatric urologic patients. A single injection of local anesthetic provides 4 to 5 hours of analgesia as high as up to the 10th thoracic dermatome (T10). The addition of ketamine or clonidine can prolong it up to 9 hours. Neuraxial

opioids prolong the duration of block up to 24 hours but increase the risk of respiratory depression so it is necessary to admit these patients for monitoring. Other side effects include pruritus and nausea.

Fig. 27-2 Wong-Baker pain rating scale. (From Wong DL, Hockenberry-Easton M, Wilson D, et al. *Wong's Essentials of Pediatric Nursing*, 6th ed. St. Louis: Mosby; 2001:1301. Copyrighted by Mosby, Inc. Reprinted by permission.)

Because the sacrococcygeal ligament progressively ossifies, the block becomes more difficult technically and has a significant failure rate after the age of 7.

Lumbar/thoracic epidural blocks with placement of a catheter for continuous infusions of local anesthetic can be done for abdominal procedures with bigger incisions when significant pain is anticipated in the postoperative period.

2. Ilioinguinal block/transverse abdominal plane (TAP) block/rectus sheath block: These are easily performed peripheral nerve blocks and the use of ultrasound affords greater accuracy with these injections. For ilioinguinal/TAP blocks, local anesthetic is injected between the transversus abdominis and internal oblique muscles. These blocks are helpful for lower abdominal incisions. In the case of a periumbilical incision, injection of local anesthetic in the posterior rectus sheath is the preferred choice.

3. Penile block: This block can provide analgesia for circumcision or hypospadias repair. The most common technique involves injection of local anesthetic at the base of the penis deep to Buck's fascia on either side of the suspensory ligament; a potential drawback to this method is that this does not provide blockade of the genitofemoral and ilioinguinal nerves that provide sensation to the base of the penis. Alternatively, the Dalens method involves infiltration of local anesthetic into the subpubic space, blocking the nerves before their entry into the penis. This also theoretically decreases the risk of injury to neurovascular or other penile structures. A third method entails a subcutaneous ring-block at the base of the penis, which also avoids trauma to important structures while still providing analgesia along the entire shaft.

B. **Systemic Agents**

Narcotics are the traditional cornerstone of pain management. They can be administered intravenously (morphine) or orally (oxycodone). Their safety and efficacy in children when used in appropriate doses is well established. Patient-controlled analgesia (PCA) can be used when the child understands and is able to use it (typically at the age of 5 or older). The current trend is to limit the use of opioids, however, due to their multiple side effects (respiratory depression, nausea, ileus, pruritus, tolerance).

1. Nonsteroidal anti-inflammatory drugs (NSAIDs): IV (ketorolac) or PO (ibuprofen) NSAIDs can be used in children over 6 months of age (several trials have established their safety when used for a short period of time). Although the evidence for their safety in healthy patients 1 to 6 months of age is limited, most children's hospitals feel comfortable using a single dose in this population. Ketorolac (Toradol) is a frequent favorite in urologic surgery as it has a strong

analgesic effect with minimal side effects. Ketorolac usually allows opiate use to be reduced or eliminated, thereby reducing opiate side effects. In addition, ketorolac is effective in reducing bladder spasms, a common problem in children who have catheters postoperatively. Because NSAIDs inhibit renal prostaglandin synthesis, they should be used cautiously in patients with renal failure or if administered concomitantly with nephrotoxic drugs (e.g., intravenous gentamicin and ketorolac probably should not be given too close to one another). In addition, the NSAIDs inhibit platelet function that, in theory, can be dangerous in any patient at increased risk for bleeding intra- or postoperatively.

2. Acetaminophen: This is a very widely used drug, especially for pain control at home. Because of its ability to decrease opioid requirements, its ease of administration (p.o. if appropriate, p.r. is an alternative), as well as its low side-effect profile, it should probably always be included as part of any analgesia plan unless significant hepatic disease is present. To get the most advantage possible from this drug, it is important to prescribe it on an "around the clock" basis and not p.r.n. An IV formulation is now available as well, but due to its expense it should be used primarily when other alternatives are not possible.

C. **Non-pharmacologic Adjuncts**

Never forget the importance of therapeutic maneuvers not found in the Physicians' Desk Reference (PDR)—cuddling with a parent may often turn a crying, inconsolable child into a cooperative, sleepy, adorable toddler. Other things to try include gentle heat therapy at the site of discomfort, distraction techniques (with games, toys, Nintendo, etc.), massage therapy, low stimulation environments (i.e., minimal lighting, sounds, and manipulation), and even comfort foods (if medically

allowed).

V. CONCLUSION

A happy and pain-free child with satisfied patients should be the goal after every surgical procedure. To achieve this end, it is important for the surgeon, parents, anesthesiology staff, and nursing staff to work together to optimize their roles and thus optimize patient care.

RECOMMENDED READING

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Pinyavat T, Warner DO, Flick RP, *et al*. *J Neurosurg Anesthesiol* 2016 Oct.;28(4):356–360.

http://smarttots.org/http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm533346.htm 2016 Summary of the Update Session on Clinical Neurotoxicity Studies.

28 Sports Recommendations for Children with a Solitary Kidney or Other Genitourinary Abnormalities

Jack S. Elder

I. OVERVIEW: SPORTS-RELATED INJURIES IN CHILDREN

Adequate data on the risks of a particular sport for an athlete with a medical problem are limited or lacking, and an estimate of risk becomes a necessary part of medical decision-making.

A. There are more than 3,000,000 annual sports-related injuries in the United States, and 65% are in the pediatric population.

B. In past legal decisions, athletes have been permitted to participate in sports despite known medical risks (AAP, 1994). When an athlete's family disregards medical advice against participation, the physician should ask all parents or guardians to sign a written informed consent statement indicating that they have been advised of the potential dangers of participation and that they understand them. The physician should also document, with the child's signature, that the child athlete also understands the risks of participation (AAP, 2001). Since 2001 there have been no updated American Academy of Pediatrics (AAP) recommendations.

II. RENAL CONDITIONS WITH INCREASED RISK OF GENITOURINARY INJURY DURING SPORTS PARTICIPATION

A. **Solitary Functioning Kidney**
   1. Typically has compensatory hypertrophy, thereby increasing the risk of injuring the kidney, because it is not as well protected by the ribs; the majority of solitary kidneys are right-sided, and the right kidney usually displaced inferiorly by the liver.
   2. Renal agenesis: incidence as high as 1 in 1,000; male:female ratio 1.8:1; left side more commonly affected; contralateral vesicoureteral reflux in 20%.
   3. Multicystic dysplastic kidney: nonfunctioning kidney with multiple cysts; incidence 1 in 1,000 to 1,500; contralateral renal abnormality in 20% to 30%, including vesicoureteral reflux and hydronephrosis; may involute and be mistaken for renal agenesis.
   4. S/P (status post) nephrectomy for tumor (e.g., congenital mesoblastic nephroma, Wilms' tumor, multilocular cystic nephroma, renal cell carcinoma) or nonfunctioning or poorly functioning kidney (ureteropelvic junction [UPJ] obstruction, ureterovesical junction obstruction, vesicoureteral reflux, renal vein thrombosis).

B. **Hydronephrosis**
   1. Anomalous UPJ or UPJ obstruction
   2. Ureterovesical junction obstruction
   3. Vesicoureteral reflux

C. **Anomalies of Renal Position**
   1. Horseshoe kidney: incidence 1 in 450; male:female ratio 2:1; most common renal fusion anomaly; isthmus inferior to inferior mesenteric artery; hydronephrosis common; unilateral multicystic dysplasia more common than in general population.
   2. Other renal fusion anomalies: estimated incidence 1 in 1,000; male:female ratio 2:1; crossed fused ectopia, with or without renal fusion: left crossing to right side accounts for two-thirds of cases; sigmoid kidney, lump kidney, and disc kidney uncommon.
   3. Renal ectopia: pelvic, lumbar; more common on left.

4. Renal transplant: pelvic position.

D. **Abnormal Renal Size**
   1. Autosomal recessive polycystic kidney disease: survival beyond infancy uncommon, but kidneys are very large.
   2. Autosomal dominant kidney disease: typically diagnosed in adulthood, but affected children typically have hypertension, proteinuria, and renal enlargement.
   3. Angiomyolipoma associated with tuberous sclerosis; both kidneys typically affected.

E. **Reduced Renal Function**
   1. Renal disease: glomerulonephritis, renal cystic disease.
   2. Renal dysplasia: may or may not be associated with vesicoureteral reflux.

III. ABDOMINAL CONDITIONS ASSOCIATED WITH INCREASED RISK OF GENITOURINARY INJURY DURING SPORTS PARTICIPATION

A. Prune belly syndrome: lax abdominal musculature predisposes to injury of solid abdominal organs as well as fluid-filled organs (e.g., bladder) from blunt trauma.

B. S/P augmentation cystoplasty or construction of urinary neobladder with continent diversion, for example, in children with bladder exstrophy, VATER (vertebrae, anus, trachea, esophagus, renal) syndrome, spina bifida.

IV. CONDITIONS WITH INCREASED RISK OF INFERTILITY FROM TESTICULAR INJURY DURING SPORTS PARTICIPATION

A. **Solitary Functioning Testis; Typically the Solitary Testis Exhibits Compensatory Hypertrophy**
   1. Secondary to in utero torsion; left side affected in two-thirds.
   2. Secondary to postnatal testicular torsion; most

common in adolescence.
3. Following removal of testicular tumor.
4. Following removal of testis from trauma.
5. Following unsuccessful orchiopexy.

B. **Undescended Testis: Incidence 1 in 60 to 100**
1. Unilateral: fertility typically nearly normal, most probably because unaffected testis is functioning normally.
2. Bilateral: fertility approximately 30% to 70%, in part because of impaired germ cell development, and in some cases because of intraoperative iatrogenic testicular or spermatic cord injury.

V. RECOMMENDATIONS OF THE AMERICAN ACADEMY OF PEDIATRICS COMMITTEE ON SPORTS MEDICINE AND FITNESS REGARDING SPORTS PARTICIPATION FROM (2001) [HAS NOT BEEN UPDATED]

A. **Classified Sports by Level of Contact**
1. Collision or contact: in collision sports, athletes purposely hit or collide with each other or with inanimate objects, including the ground, with great force; in contact sports, athletes routinely make contact with each other or with inanimate objects, but usually with less force than in collision sports; include basketball, boxing, diving, field hockey, tackle football, ice hockey, lacrosse, martial arts, rodeo, rugby, ski jumping, soccer, team handball, water polo, wrestling.
2. Limited contact: contact with other athletes or inanimate objects is infrequent or inadvertent; includes baseball, bicycling (competitive bicycle racing not listed separately), cheerleading, canoeing or kayaking (white-water), fencing, field events (high jump, pole vault), floor hockey, flag football, gymnastics, handball, horseback riding, racquetball, skating (ice, in-line, roller), skiing (cross-country,

downhill, water), snowboarding, softball, squash, ultimate Frisbee, volleyball, surfing, windsurfing.

3. Noncontact sports include all other sporting activities.

B. **Kidney, Absence of One**

1. "Qualified yes" for participation. "Athlete needs individual assessment for contact, collision, and limited-contact sports."

C. **Testicle, Undescended or Absence of One**

1. "Yes" for participation. "Certain sports may require a protective cup."

VI. ATTITUDES OF PEDIATRIC UROLOGISTS (2002) AND PEDIATRIC NEPHROLOGISTS (2006) REGARDING SPORTS PARTICIPATION BY CHILDREN WITH A SOLITARY KIDNEY

A. Sharp et al. (2002) surveyed 231 members of the American Academy of Pediatrics, Section on Urology; 182 (79%) responded.

1. Participation in contact sports was strongly advised against by 68% (contact sports not defined)?
2. What is advice to patient?

   Strongly advise against participation: 26%.
   Recommend against participation with exception for highly skilled or motivated patient: 30%.
   No recommendation either way: 14%.
   Recommend allowing participation: 25%.
   Feel strongly that patient should have no restrictions: 4%.

   Note that recommendations to questions 1 and 2 were inconsistent.

3. Flank protectors were recommended by 71%, even if not normally used for that sport.

B. Grinsell et al. (2006) surveyed 430 members of the American Society of Pediatric Nephrology; 135 (31%) responded.

1. Of those who responded, 62% "would not allow" contact/collision sports by patients with a normal solitary kidney.

a. Of those who would allow contact sports, 86% recommended avoiding American football, 75% boxing, 70% ice hockey, 64% rugby, 60% martial arts, and 54% rodeo.
b. Downhill skiing and bicycling least likely for limited participation.
c. Only 5% referred to 2001 AAP statement as justification.

2. Of those who would allow participation, 54% recommended additional protective equipment.
3. Recommendation that families sign a waiver indicating that they understood the risk of a sports injury was done by 37%.
4. Conclusion: Current practice patterns of physicians and the recommendations of the AAP would benefit from reevaluation, modification, and clarification to help families make reasonable choices for their children.

VII. DATA PERTAINING TO RENAL TRAUMA FOLLOWING SPORTS INJURY

A. Gerstenbluth et al. (2002): Reviewed 68 children with blunt renal trauma, mean age 10 years.
1. Twenty (29%) associated with recreational sports: 8 bicycling; hockey, all-terrain vehicle 3 each; horse kick, sledding 2 each; football, jet ski 1 each.
2. Injury severity score mean 20.6 for bicycle injury and 6.7 for nonbicycle sports–related trauma ($p < 0.05$).
3. Bicycle injuries: none involved collision with vehicle; 1 grade III, 2 grade IV, 3 grade V renal injuries; 1 nephrectomy for life-threatening hemorrhage.
4. Hockey 1 grade II, 1 grade III, 1 grade IV; sledding 1 grade I, 1 grade II; football 1 grade I.
5. Conclusion: bicycling most common sports-related cause of renal injury. Team contact sports uncommon risk factor.

B. McAleer et al. (2002): Reviewed 14,763 patients in San Diego trauma registry from 1984 to 2000; identified 193 renal injuries.
    1. Sixty-nine (36%) associated with recreational sports: 27 bicycling; playground equipment, all-terrain vehicle 8 each; skateboarding, rollerblading 6 each; 4 playing ball; 3 equestrian; 1 trampoline; 6 team sports. Outcomes focused on team sports.
    2. Team sports: football 2 contusions, 1 fracture; soccer 1 contusion with UPJ obstruction; basketball 1 hematoma, 1 contusion.
    3. Team sport injury for overall series 3.4%, versus 0.04% for renal injury.
    4. Conclusion: recommendations against team sport participation may not be necessary in patients with a solitary kidney or testis.
C. Johnson et al. (2005): Analyzed data from 49,651 pediatric trauma cases collected by 92 trauma centers from 1995 to 2001 as part of the National Pediatric Trauma Registry.
    1. In sports group, 4 nephrectomies; associated with sledding 2, skiing 1, and rollerblading 1.
    2. In nonsports/other group, 3 nephrectomies, all from equestrian activities.
D. Grinsell et al. (2012): Reviewed data from the National Athletic Trainers' Association (NATA) from 1995 to 1997; 4.4 million athlete exposures.
    1. Out of 23,666 injuries 18 (0.07%) were renal; 3 lacerations, none required surgery, no renal loss; 15 occurred in boys, 3 in girls.
    2. Rate of renal injury per 1,000,000 exposures: baseball 3.2, basketball 2.3, football 9.2, soccer 2.6.
    3. In comparison, 3,500 knee injuries and 1,200 brain injuries.
E. Brophy et al. (2008): Reviewed National Football League renal injuries from 1986 to 2004.
    1. Total of 52 injuries; 6 kidney lacerations, 42

contusions, 2 kidney stones, 2 kidney dysfunction (unrelated to trauma).
2. None underwent nephrectomy.
3. Rate of kidney injury during games 0.000055 per exposure.

F. Psooy (2014): Reported Canadian Urological Association Guidelines on sports and the solitary kidney.
1. Most evidence pertaining to renal trauma and sports/recreational activity is Level 3.

VIII. SUMMARY OF DATA PERTAINING TO RENAL TRAUMA FROM RECREATIONAL SPORTS

A. Highest risk of renal trauma from bicycling, American football, skiing (including snowboarding and sledding), ice hockey, and equestrian.
B. Risk of renal injury secondary to sports variable by regional preferences for recreational activities.
C. In contact sports, risk highest in American football, but significantly lower compared to bicycling and skiing.
D. Girls at low risk of kidney injury during contact sports.

IX. OTHER CONSIDERATIONS REGARDING RENAL TRAUMA IN CHILD WITH SOLITARY KIDNEY

A. In a large series of pediatric trauma, renal injury resulted from motor vehicle injury (child either patient or pedestrian) in 17% to 77% and from fall in 6% to 50%. Overall, sports-related causes contributed to only 10% of renal trauma.
B. Although kidney is the most commonly injured organ in blunt abdominal trauma, head injuries are significantly more common. The risk of contact sports includes participation with a solitary liver, spleen, and brain. Although only 10% of head injuries are related to sports, head injuries cause 70% of traumatic deaths and 20% of permanent disability in sports.

C. Nephrectomy or significant renal impairment is unusual following blunt renal injury.
D. In a child with solitary kidney, the kidney typically is significantly enlarged, whereas in clinical series of children with renal trauma, nearly all have two normal kidneys.
E. Renal loss from sports activity in a child with UPJ obstruction and blunt trauma not reported.
F. No reports in medical literature of loss of solitary kidney from trauma.
G. Virtually all reports of renal injury from team sports in boys.
H. Loss of solitary kidney to blunt trauma from contact sport would be devastating.
I. No recent data on risk of renal injury in pediatric patients with renal/urinary tract anomaly (UPJ obstruction, ectopic kidney, cross-fused ectopia, augmentation cystoplasty).
J. Flank pads and belts are available to protect against urologic injuries. However, they have not been tested formally and do not conform to any standard in regard to degree of protection (Papagiannopoulos and Gong [2016]).

X. RECOMMENDATIONS REGARDING LIMITATIONS IN CHILD OR ADOLESCENT WITH SOLITARY KIDNEY OR RENAL ABNORMALITY

A. Advise patient and family that risk of injury is highest with bicycling, American football, skiing (including snowboarding and sledding), ice hockey, and equestrian. However, risk of renal injury from sports accounts for approximately 0.05% of pediatric trauma.
B. Advise that risk in girls participating in team sports appears extremely low.
C. Advise against extreme sports involving bicycles.
D. Advise that flank protectors are available, but are not standardized.
E. Advise against collision sports in children with renal

fusion abnormality, prune belly syndrome, augmentation cystoplasty, or renal transplant.

F. Document discussion with patient and family carefully in medical record. Option: ask the family to sign a document regarding the discussion.

XI. DATA PERTAINING TO TESTICULAR TRAUMA FOLLOWING SPORTS INJURY

A. McAleer et al. (2002): Reviewed 14,763 patients in San Diego trauma registry from 1984 to 2000; identified 11 testis injuries from recreational sports; analysis focused on team sports.
   1. Cause of testicular injury: 4 team sports (2 baseball, 1 basketball, 1 soccer); playing ball, playing on playground equipment 2 each; 1 rollerblading; 1 bicycling; 1 equestrian sports.
   2. Of 4 testicular injuries from team sports, 2 fractures and 2 hematomas. All were explored and none sustained testicular loss.

B. Grinsell et al. (2012): Reviewed data from the National Athletic Trainers' Association (NATA) from 1995 to 1997; 4.4 million athlete exposures.
   1. Seventeen testis injuries (compared to 18 reported kidney injuries); 1 basketball, 12 American football, 3 soccer, 1 wrestling,
   2. Rate of testicular injury per 1,000,000 exposures: baseball 0, basketball 2.3, football 9.2, soccer 7.8, wrestling 1.9.

C. Bagga et al. (2015): Reviewed data from the National Electronic Injury Surveillance System from 2002 to 2010; identified children below 18 years of age who presented to emergency departments with a pediatric genitourinary injury in the United States.
   1. Most common causes of scrotal injury were bicycling (24.7%), baseball/softball (13.5%), basketball (8%), American football (7.8%), exercise equipment (6.3%), and soccer (6.1%).

2. Three times as many testicular injuries present to emergency department (ED) as do kidney injuries.

D. Bieniek and Sumfest (2014): Surveys distributed to 1,700 male high-school and college athletes, age 14 to 24 years, regarding self-reported testicular injuries and the use of protective equipment; 731 surveys completed (43% response rate).
   1. Testicular injury defined as "testicular pain during an injury occurring during sports, whether seen by a physician or not." No data on ED visit, surgical treatment.
   2. Rate of testicular injury: baseball 21%, basketball 11.8%, American football 17.8%, lacrosse 48.5%, soccer 25.6%, wrestling 32.8%.
   3. Rate of protective cup use: baseball 40.6%, basketball 2.6%, football 8.4%, lacrosse 51.5%, soccer 2.4%, wrestling 0%.
   4. If testicular injury was without wearing a cup, is a cup worn now? Baseball 48.3%, basketball 0%, football 8.2%, lacrosse 68.8%, soccer 0%.

E. No national (United States) standard regarding use of protective equipment to prevent testicular injury.

XII. RECOMMENDATIONS REGARDING LIMITATIONS IN CHILD OR ADOLESCENT WITH SOLITARY TESTIS OR ABNORMAL TESTIS

A. Advise patient and family that reports of testicular injury uncommon from sports participation, but that lack of reports probably results from many male athletes wearing protective cup.

B. Recommend use of protective cup in boys participating in contact sports.

C. Document discussion with patient and family carefully in medical record. Option: ask the family to sign a document regarding the discussion.

RECOMMENDED READING

American Academy of Pediatrics, Committee on Sports Medicine and Fitness. Medical conditions affecting sports participation. *Pediatrics* 1994;94:757–760.
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29 Pediatric Urology and Child Sexual Abuse

Angelique M. Champeau

I. INTRODUCTION

Due to the large number of children who have been and/or will be sexually abused, it is important for all medical practitioners caring for children to be well informed with regard to child sexual abuse. More specifically, some children who have been sexually abused may manifest this abuse with urologic conditions, such as incontinence. Moreover, children may be referred for concerns of child sexual abuse for a non-abuse urologic condition, such as urethral prolapse. In addition, in the process of examining a child's genitalia for a urologic condition unfamiliar findings may be revealed; therefore, it is important to understand the normal and potentially abnormal findings of the genital exam.

II. DEFINITION

According to the World Health Organization (WHO): The involvement of a child in sexual activity that he or she does not fully comprehend, is unable to give informed consent to, or for which the child is not developmentally prepared and cannot give consent, or that violate the laws or social taboos of society. Child sexual abuse is evidenced by this activity between a child and an adult or another child who by age or development is in a relationship of responsibility, trust or

power, the activity being intended to gratify or satisfy the needs of the other person. This may include but is not limited to: the inducement or coercion of a child to engage in any unlawful sexual activity; the exploitative use of child in prostitution or other unlawful sexual practices; the exploitative use of children in pornographic performances and materials.

III. EPIDEMIOLOGY

A. The 2006 World Report on Violence against Children provided estimates that in 2002 approximately 150 million girls and 73 million boys were subject to child sexual abuse worldwide, including 1.2 million trafficked children and 1.8 million exploited through prostitution or pornography.

B. In the United States, a population-based sample of face-to-face interviews with more than 34,000 adults found that 10% of respondents reported experiencing child sexual abuse before age 18 years, 25% of whom were men.

C. One meta-analysis of global prevalence studies included 65 articles involving 37 male and 63 female samples across 22 countries, totaling more than 10,000 individuals. The investigators reported a combined mean prevalence of child sexual abuse in 7.9% of males and 19.7% of females.

D. Another meta-analysis included data from 331 studies representing nearly 10 million individuals. In this analysis, the total combined prevalence was 11.8%, with 7.6% of males and 18% of females reporting experiences of child sexual abuse.

E. Children are more frequently abused by males; however, women may be perpetrators, especially in day care settings.

F. Most perpetrators of sexual abuse are trusted adult acquaintances of the child, who often target children lacking close adult supervision and craving adult

attention.

IV. RISK FACTORS

A. Presence of other forms of abuse or neglect
B. Family environments with low family support and/or high stress, such as high poverty, low parental education, absent or single parenting, parental substance abuse, domestic violence, or low caregiver warmth.
C. Children who are impulsive, emotionally needy, and who have learning or physical disabilities, mental health problems, or substance use
D. The risk of child sexual abuse appears to increase in adolescence.
E. Out-of-home youth may be particularly at risk
F. Children in conflict with the law may be at risk of abuse by authorities both on the street and in detention
G. Children living in conflict and post conflict environments

V. PRESENTATION

A. Children who are sexually abused are generally coerced into secrecy, therefore a high index of suspicion is required to recognize the problem.
B. Children who have been sexually abused may present in a variety of ways.
    1. History
        a. Genital/rectal complaints (Table 29-1).
        b. A parent may communicate concerns that the child has been sexually abused.
        c. The child may actually make an initial disclosure of sexual contact at a medical visit (rare).
        d. Behavioral and emotional problems may raise concern, although it is important to keep in mind that these are nonspecific and may be related to many other causes.

TABLE Possible Medical Indicators of Sexual Abuse

29-1

Genital, anal, or urethral trauma
Genital or anal bleeding or itching
Genital infection or discharge
Headaches
Chronic constipation, painful defecation
Vulvitis or vulvovaginitis
Pregnancy
Foreign body in the vagina or rectum
Anal inflammation
Dysuria
Recurrent UTI
Abdominal pain
Chronic genital or anal pain
Bruises to hard or soft palate, torn frenulum
Sexually transmitted disease
Bite marks on nipples/breasts
Scratch marks or bruises on hips/buttocks
Enuresis/encopresis

2. Physical examination
   a. During examination of the genitalia, suspicious findings may be observed.

VI. HISTORY

A. In legally proven cases of child sexual abuse, the majority of victims have no diagnostic physical findings. Therefore, the unbiased interview of the child becomes the most critical part of the diagnostic evaluation. Investigative interviews should be conducted by the designated agency or individual in the community to minimize repetitive questioning of the child. However, one should not hesitate to ask relevant questions needed for a detailed pediatric history.

B. Any spontaneous disclosure by the child during the assessment must be documented carefully and thoroughly

using the exact terminology that the child used. *Although hearsay evidence is typically inadmissible in court, statements made to a doctor in the course of a medical evaluation are generally recognized as reliable and are an important exception to the hearsay rule.*

VII. PHYSICAL EXAMINATION

A. General Examination

1. A more general physical examination should be done prior to the genital examination. Always discuss the genital examination prior to initiating. Older children should be given the choice of whether they would like their parent to be present or not. Provide for privacy. After the routine physical examinations, the genital examination should be prefaced with a (age-appropriate) statement such as, “I am now going to examine the hole where the pee comes out, it is ok for me to do this because your caregiver is in the room and I am a medical professional at a medical office/hospital, otherwise no one should look or touch your private area.” If sexual abuse is a concern, finish this statement with, “Has anyone ever tried to touch you here before.” Making the first statement *every time* one examines a child’s genitalia allows the statement to feel very comfortable and normal for a child, and when the second statement is needed, it will also feel more comfortable. A certain level of comfort and confidence is important for the genital examination. Although a child might not answer honestly initially, if all medical professionals ask these questions, eventually we hope they might. Try to use distraction and relaxation during the examination. Note the child’s behavior during the examination. *No child thought to have been sexually abused should ever be forcibly restrained and examined against his/her will; arrangements should be made for an examination under anesthesia.*

2. Examination findings change depending on the position of the child (supine, knee chest, lateral), degree of relaxation, amount of labial traction (gentle, moderate), and time of performing the examination. All these variables will influence the size of the orifice and the exposure of the hymen and the internal structures. The more relaxed the child is, the more visible the hymenal edges and the more dilated the introitus diameter; therefore, it is very important to view findings using varying traction and varying positions.
3. In females, the genital examination should include inspection of the medial aspects of the thighs, labia majora, labia minora, clitoris, urethra, periurethral tissue, hymen, hymenal opening, fossa navicularis, and posterior fourchette/posterior commissure (Fig. 29-1). In male children, the urethral meatus, thighs, penis, and scrotum should be examined.

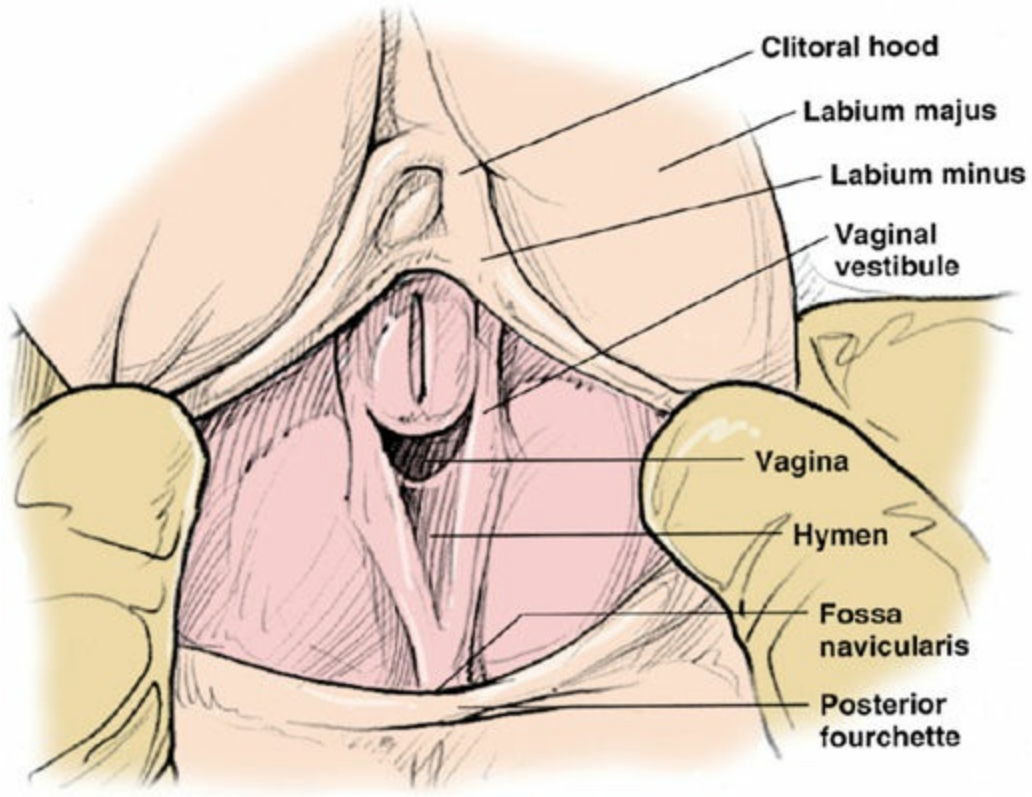

Fig. 29-1 Anatomy of prepubertal female genitalia.

4. In prepubertal girls, a pelvic examination with a speculum is unnecessary, unless there is unexplained active vaginal bleeding.

B. **Examination Positions**

1. Supine frog-leg position (Fig. 29-2)

Fig. 29-2 Supine frog-leg position.

a. Child lies with legs in full abduction "like a frog" with feet in apposition. In younger children, seating the child in the caretaker's lap may facilitate the examination.
b. Examine first without separation or traction, and then with simple separation (where the labia is separated laterally only).
c. Labial separation should be done gently and with caution. Labial separation can be painful and may cause tears of the posterior fourchette/commissure. If a labial adhesion is present, aggressive labial separation may tear it.
d. Gentle traction (Fig. 29-3) should then be applied by placing the thumb and forefinger on the labia majora and pulling laterally and downward. Tension of the other pelvic muscles

can obscure and/or change the view of the vaginal vestibular structures, therefore maintain labial traction for a few seconds allowing the child time to relax. This method is successful in opening the vaginal canal without causing additional trauma to the tissues.

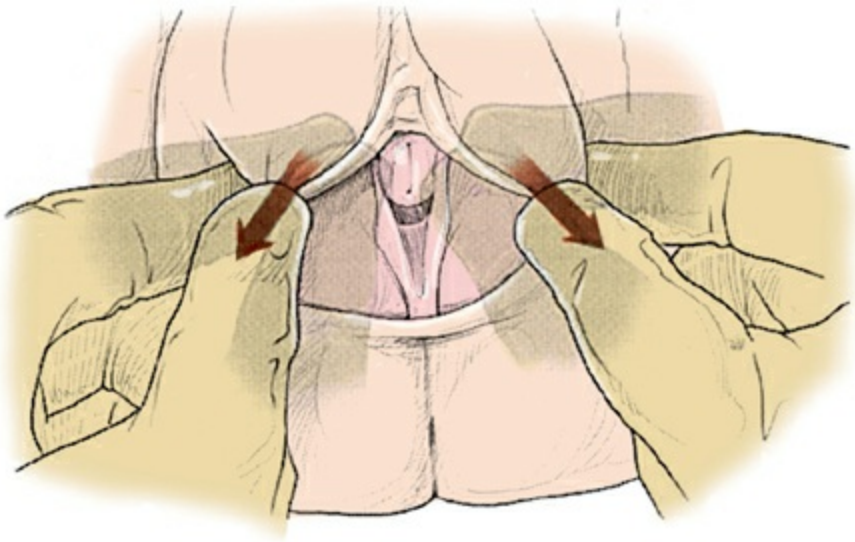

Fig. 29-3 Labial traction.

2. Knee-chest position (Fig. 29-4)

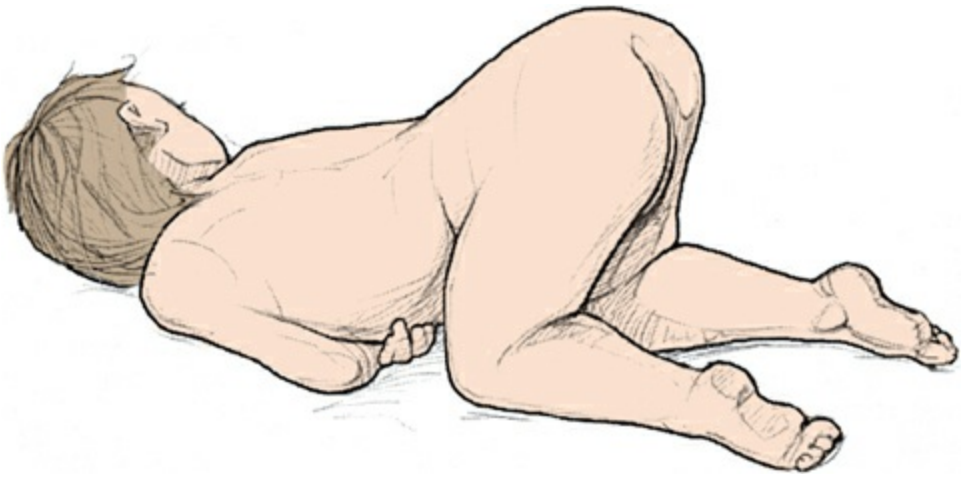

Fig. 29-4 Knee-chest position.

a. Instruct the child to lie prone on the examining table. Then assist the child to assume a kneeling

position while he or she maintains head and chest contact with the table and lordosis of the back. Once the child is positioned properly, lift the labia upward and apart gently.

b. This technique allows excellent noninvasive visualization of the posterior hymen, vagina, anus, and occasionally the cervix.
c. This position may allow previously adhered and possibly redundant hymenal tissue to drop downward.
d. Use this examination position routinely to clarify questionable examination findings, and to verify normal or abnormal findings first noted when the patient is supine.
e. In cases where there is bleeding or suspicion of vaginal foreign body, this position is helpful in that it can provide visualization of the cervix.

C. **Examination Techniques**

1. Saline/water
   a. Redundancy of estrogenized postpubertal hymen makes close inspection of the hymenal tissues for traumatic injury difficult in adolescents.
   b. If the hymenal edges are difficult to visualize, warm normal saline drops or water may be used in order to float the hymen without any discomfort to the child.
2. Moistened swab
   a. A moistened swab may be used to trace the edges of the hymen.
   b. The hymenal edge is very sensitive in prepubertal girls, therefore every effort should be made to visualize the genitalia without using a swab. If a swab is needed to explore the hymenal margin in a prepubertal child, then 2% Lidocaine topical gel can facilitate use of the swab. The estrogenized hymen is much more tolerant of the moistened swab.

3. Foley catheter
    a. The catheter is inserted into the vagina, the balloon is then inflated partially, and then the catheter is slowly pulled until the entire hymen can be visualized around the balloon. The balloon should be deflated prior to removal from the vagina.
4. Magnification
    a. An otoscope or other handheld magnification can also be used to examine the genitalia and the anus.
    b. Colposcopy is the use of magnification and photographic and/or videographic documentation of physical findings of suspected sexual abuse. It has become routine practice for sexual abuse examinations done by experts; however, it is not a common piece of equipment in most medical practices, and is not recommended.

D. **Anal Examination**

1. The anus can be examined in the supine, lateral, or knee-chest position (Fig. 29-5). As with the vaginal exam, position may influence anatomy. Gluteal folds should be gently separated and assessed for external signs of trauma and to assess if anal dilation will occur. Apply greater traction thereafter in an effort to inspect the anus thoroughly. Only if there is rectal bleeding is an endoscopic examination indicated. Digital rectal examination is generally not indicated.

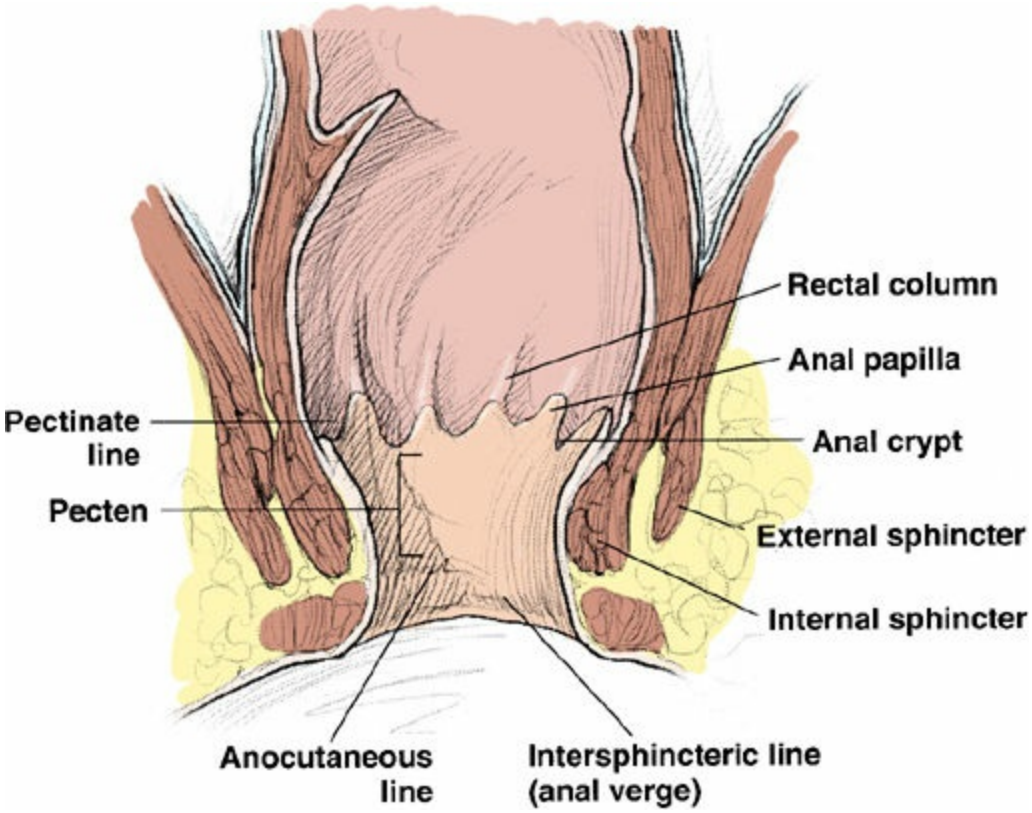

Fig. 29-5 Anatomy of the anus.

E. **Documentation**

1. All physical findings should be clearly documented in the child's medical record.
2. Hymenal and/or anal findings should be documented using the o'clock designations (i.e., "at 6:00 in the supine, frog-leg position using labial traction").
3. Whenever possible a drawing should be used.
4. For those with limited sexual abuse training it is best to describe the finding in detail and not comment on whether the finding is consistent with abuse or not.
5. Never write "hymen intact," "no signs of penetration," or "no evidence of sexual abuse" because even a normal physical examination does not rule out the possibility of sexual abuse, including penetration.

F. **Examination Findings**

1. Normal hymenal variations
   a. Most common

(1) Crescentric: Attachments at approximately the 11 o'clock and the 1 o'clock positions without hymenal tissue between the two attachments.
(2) Annular hymen: The tissue membrane extends completely around the circumference of the entire vaginal orifice.

b. Less common
(1) Cribriform: A hymen with multiple small openings.
(2) Imperforate: The hymenal membrane has no opening.
(3) Septate: The hymenal orifice is bisected by a band of hymenal tissue creating two or more orifices. The septate hymen should be differentiated from a bifid or duplicate vagina.

2. Variations in hymenal appearance
a. Estrogen
(1) The hymenal appearance may vary over time due to the effects of puberty or exogenous estrogen.
(2) Estrogen causes thickening of the hymenal tissue and paleness of the mucosa.

b. The opening size varies according to patient positioning, examination technique, degree of relaxation, patient's age and patient's size (generally, an obese child has a larger orifice).

c. There are a range of anatomic variants of normal prepubertal hymens (Table 29-2).

TABLE 29-2 Genital Examination Findings in Prepubertal Girls Selected for Non-abuse

More Common Findings	Less Common Findings

Erythema of the vestibule	Posterior fourchette friability
Periurethral bands	Hymenal clefts
Lymphoid follicles on the fossa navicularis	Imperforate hymen
Labial adhesions	Hymenal septa
Posterior fourchette midline avascular areas	Vaginal discharge
Urethral dilation with labial traction	Foreign body
Projections: septal remnants, hymenal tags, mounds	
Vaginal ridges	
Rugae	

d. Newborn

(1) The normal newborn hymen is generally thickened and redundant and may be described as fimbriated. By 3 years of age, the majority of girls have developed a thin crescentric hymen, some with annular hymen.

G. **Physical Findings of Sexual Abuse**

1. Sexual abuse in children will often leave no physical findings for the following reasons.
   a. Perpetrators will often befriend and avoid physical injury to the child.
   b. Digital fondling can occur without tissue damage.
   c. The vaginal vestibular tissues are very elastic.
   d. Genital tissues heal rapidly and often heal completely.
   e. The anus can easily stretch without causing tissue damage.
   f. Early pubertal estrogen effects increase hymenal elasticity, hymenal redundancy, and physiologic vaginal secretions, all of which lessen the likelihood of traumatic hymenal tearing.

g. Hymenal defects become less visible following puberty.
h. Some children who have normal genital examinations disclose penile penetration that is verified independently by confession or conviction of the perpetrator.

2. Consistent with but *not* diagnostic of abuse include the following.
   a. Chafing, abrasions, or bruising of inner thighs or genitalia.
   b. Scarring or tears or distortion of the hymen.
   c. Decreased amount of or absent hymenal tissue.
   d. Scarring, injury, or tears of the fossa navicularis, posterior fourchette, labia minora.
   e. Enlargement of the hymenal opening.
   f. Thickened, irregular, and/or narrowed hymen edges.
   g. Exposure of the intravaginal contents.
3. Normal congenital angular concavities or defects may be observed anteriorly, but not posteriorly. The incidence of posterior angular concavities or defects increases with age, suggesting acquired lesions. Physical examination for sexual abuse in females should focus on the posterior vestibular structures.
4. Abnormal findings are rarely noted in sexually abused boys. If present, these findings most often involve the anus and are easily seen with careful inspection. Penile or scrotal injuries are uncommon.
5. Acute anal findings in either sex can include bruises around the anus, swelling, redness, abrasions, scars, anal tears (especially those that extend into the surrounding anal perianal skin), and occasional fissures extending to the anal verge. If present, laxity of the sphincter should be noted. These superficial injuries heal rapidly. It is unusual to find rectal lacerations from forceful penetration. These deeper injuries occasionally heal as scarring, which may

become less visible with time. Anal lacerations often do not leave scars. Anal findings suggestive of chronic repetitive trauma can include anal deformities or “tags” outside the midline. Dilation greater than 15 mm that occurs within 30 seconds without stool in the ampulla or a marked thickening and irregularity of anal folds after complete dilation. Table 29-3 lists the classification of physical findings.

TABLE 29-3 Classification of Physical Findings

Findings specific/diagnostic for sexual contact (even in the absence of a history of abuse)

- Evidence of ejaculation (semen, sperm, or semen-specific antigens and/or enzymes)
- Pregnancy
- Syphilis, gonorrhea, or HIV infection not acquired perinatally or intravenously
- Fresh genital or anal injuries in the absence of an adequate accidental explanation:

laceration, hematoma, ecchymoses, bite mark, abrasion, transection, contusion, petechiae

- Enlarged hymenal opening for age with associated findings of hymenal disruption in the absence of an adequate explanation: absent hymen, hymenal remnants, healed transections or scars

Findings consistent with sexual contact (history and other investigations may be important)

- Trichomonas, chlamydia, *Condylomataacuminatum*, herpes simplex virus
- Hymenal disruptions: posterior/lateral angular concavity, transection, decrease amount, scars
- Specific anal changes: anal scars or tags outside the midline, dilation greater than 15 mm without stool in the ampulla, irregularity of the anal orifice after dilation

- Marked dilation of the hymenal opening persisting in different examination positions

Findings sometimes seen following sexual contact but also following other causes (history and other investigations are important in diagnosing abuse)

- Bacterial vaginosis
- Extensive labial adhesions in girls several years out of diapers, with no other cause of labial chafing or denudation
- Posterior fourchette friability
- Other anal changes: repeated anal dilation less than 15 mm, shortening or eversion of the anal canal, perianal fissures, thickened perianal skin and reduction of skin folds
- Penile erection maintained during examination in prepubertal boys

Findings unlikely to be due to sexual contact

- Vestibular findings: lymphoid follicles or midline avascular areas of the fossa navicularis
- Urethral findings: periurethral bands, urethral dilation with labial traction
- Hymenal findings: small hymenal mounds/tags, septal remnants, anterior hymenal clefts, smooth, curved, and/or shallow, imperforate hymen
- Labial findings: small labial adhesions, extensive labial adhesions in girls in diapers, midline avascular areas to posterior fourchette
- Intravaginal ridges or rugae structures behind a normal hymen
- Anal findings: erythema, increased pigmentation, venous engorgement after 2 minutes in knee-chest position, midline skin tags/folds anterior to anus, smooth areas in midline, single episode of anal dilation less than 15 mm, anal dilation with stool in ampulla, flattening of anal verge and rugae during anal dilation
- *Candida albicans*

H. **Differentiation: Child Sexual Abuse versus Accidental Genital Injury**

1. Conditions most commonly confused with child sexual abuse include vulvovaginitis from poor hygiene, bubble baths, nonsexually transmitted infection (such as strep and shigella), foreign bodies, accidental trauma, and congenital midline structural variations.
2. Female genital trauma caused by accidental straddle injury typically affects the clitoris, clitoral hood, mons pubis, and labial structures. These structures are mostly anterior and are injured when compressed between an object and the pubic bone. Straddle injuries are usually asymmetric and do not involve the hymen.
3. When there is tissue damage resulting from penetrating sexual abuse of girls, the injuries usually involve primarily the posterior commissure, fossa navicularis, and posterior hymen. Injury is considered to have been inflicted in the absence of clear history (witnessed or immediately reported to an adult by the child) of accidental injury consistent with the child's presentation. Even in a child too young to say what happened, if there is tissue injury significant enough to cause tearing/bleeding, it is unlikely a supervising adult would not be aware of the trauma and be able to determine from environmental cues what had occurred (e.g., I heard her crying and found her straddling the toy box).

I. **Sexually Transmitted Diseases (STDs)**

1. Routine cultures and screening of all sexually abused children for gonorrhea, syphilis, hepatitis, HIV, or other STDs are not recommended. The yield of positive STDs is very low in asymptomatic prepubertal children,

especially those whose histories include fondling only. When epidemiologically indicated, or when the history and/or physical findings suggest the possibility of oral, genital, or rectal contact, appropriate tests should be obtained.

2. With genital warts there can be vertical transmission that does not manifest itself for up to 2 years or more. In addition, a child still in diapers can have transmission from the hands of a caretaker involved in diapering and hygiene. Older children can autoinoculate the genital area with warts on their fingers.
3. With herpes, type I must be differentiated from type II; however, both can be found in the genital area and both can be transmitted sexually or nonsexually.
4. The presence of vaginal discharge or history of vaginal discharge following sexual abuse increases the likelihood of STDs. Prevalence rates of STDs among sexually abused children are generally less than 4%, but vary in geography and specific STD.
5. If a culture is done, only gold-standard culture systems should be used. Nonculture tests such as direct fluorescent antibody enzyme immunoassay or DNA nucleic acid sequence should not be used; they lack adequate specificity on specimens obtained from the vagina or the anus of children.
6. Of note, the vaginal pool is an acceptable source of culture in the prepubertal child, but a cervical swab must be done for pubertal children.

J. **Acute Sexual Assault**

1. When the alleged sexual abuse has occurred within 72 hours, the examination should be done immediately by a trained sexual abuse examiner. Rape kit protocols need to be followed in order

to maintain a “chain of evidence” and is beyond the scope of routine pediatric practice.

VIII. MANAGEMENT

A. In all 50 states, physicians are mandated by law to report to Child Protection Services (CPS) or local law enforcement whenever they suspect that a child has been sexually abused. It is most helpful to have these phone numbers ready in advance for quick and easy reference. In addition to the numbers of local law enforcement and CPS the practitioner should obtain the phone number of the local child sexual abuse medical examiner. This person can be an invaluable resource with questionable examination findings.

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30 Pediatric and Adolescent Gynecology

Bruce J. Schlomer

Pediatric urologists often care for pediatric patients with abnormalities of the vagina and müllerian structures. Below is a review of some of the most common pediatric and adolescent gynecologic conditions seen by pediatric urologists.

I. INTRALABIAL ANOMALIES

A. Imperforate Hymen

Obstruction of female reproductive tract in utero is rare but is most commonly caused by imperforate hymen. This can be detected prenatally where a dilated vagina/uterus is seen as a cystic structure in the pelvis. However, the most common time for diagnosis is in the newborn period where a bulging cystic structure is seen in the posterior introitus, which typically has a whitish appearance with overlying thin membrane. Maternal estradiol exposure is what leads to the vaginal secretions. If the imperforate hymen is missed in the newborn period, the dilation may resolve as the maternal estradiol exposure ends and the patient may come back at puberty with cyclic abdominal pain, amenorrhea, and bluish bulging structure in posterior introitus (Fig. 30-1). Imperforate hymen in newborns is treated by transverse incision of the hymen. Needle aspiration is not recommended due to concerns about causing infection.

Fig. 30-1 Imperforate hymen presenting as a vaginal bulge with cyclic abdominal pain during puberty.

B. Labial Adhesions

Labial adhesions are a common finding in young children especially before the age of potty training. The fusion usually starts posteriorly and an opening remains anteriorly (Fig. 30-2). The low estrogen state and possible irritation from urine in diapers is thought to lead to these adhesions. If labial adhesions are asymptomatic, no treatment is needed, as there is a high spontaneous resolution rate. If there are symptoms such as UTI, vaginal pain/itching, or significant parental concern a 4- to 6-week course of topical estrogen or steroid cream is often successful in resolving adhesions. Lysis of adhesions in the clinic after topical anesthetic or lysis of adhesions in the operating room can also be performed. After any successful active intervention for labial

adhesions, recurrence is common and therefore a lubricating ointment such as petroleum jelly should be applied after separating labia during diaper changes for several weeks to months to prevent recurrence.

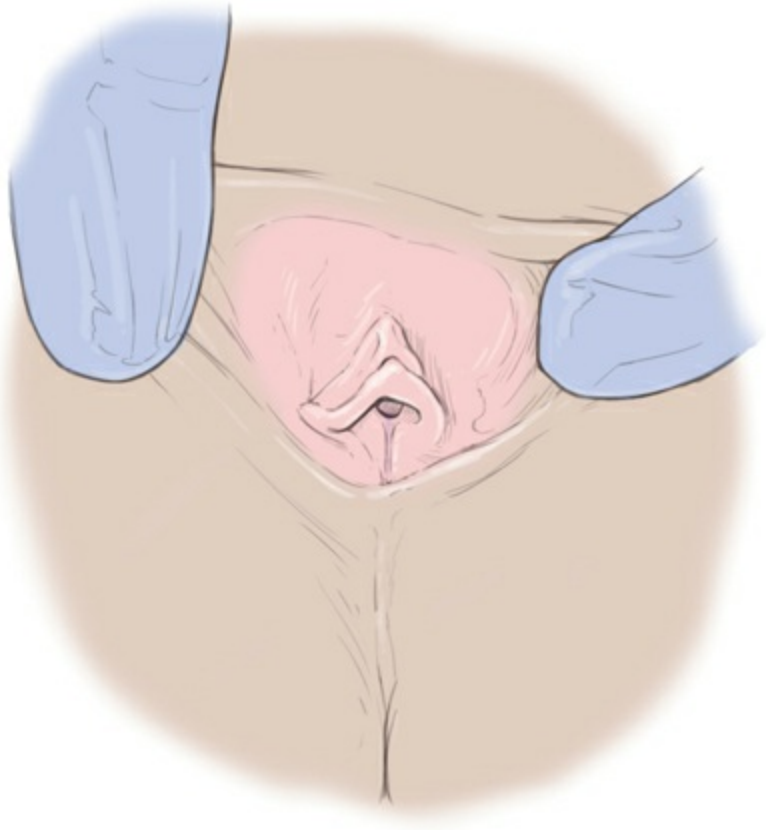

Fig. 30-2 Labial adhesions. Note the posterior labial fusion.

C. Urethral Prolapse

Urethral prolapse often presents with blood in diaper or underwear and reddish bulge in introitus circumferentially around meatus (Fig. 30-3). There may also be complaints of pain. In the pediatric age group, urethral prolapse typically occurs in prepubertal children and is most common in those of black race. As in labial adhesions, urethral prolapse is thought to be due to the low estrogen state before puberty. A 4- to 6-week course of topical estrogen cream is often successful in treating urethral prolapse, but recurrence is not infrequent. Surgical excision of prolapsed mucosa followed by

reapproximation of mucosa with absorbable sutures is sometimes required for recurrent urethral prolapse.

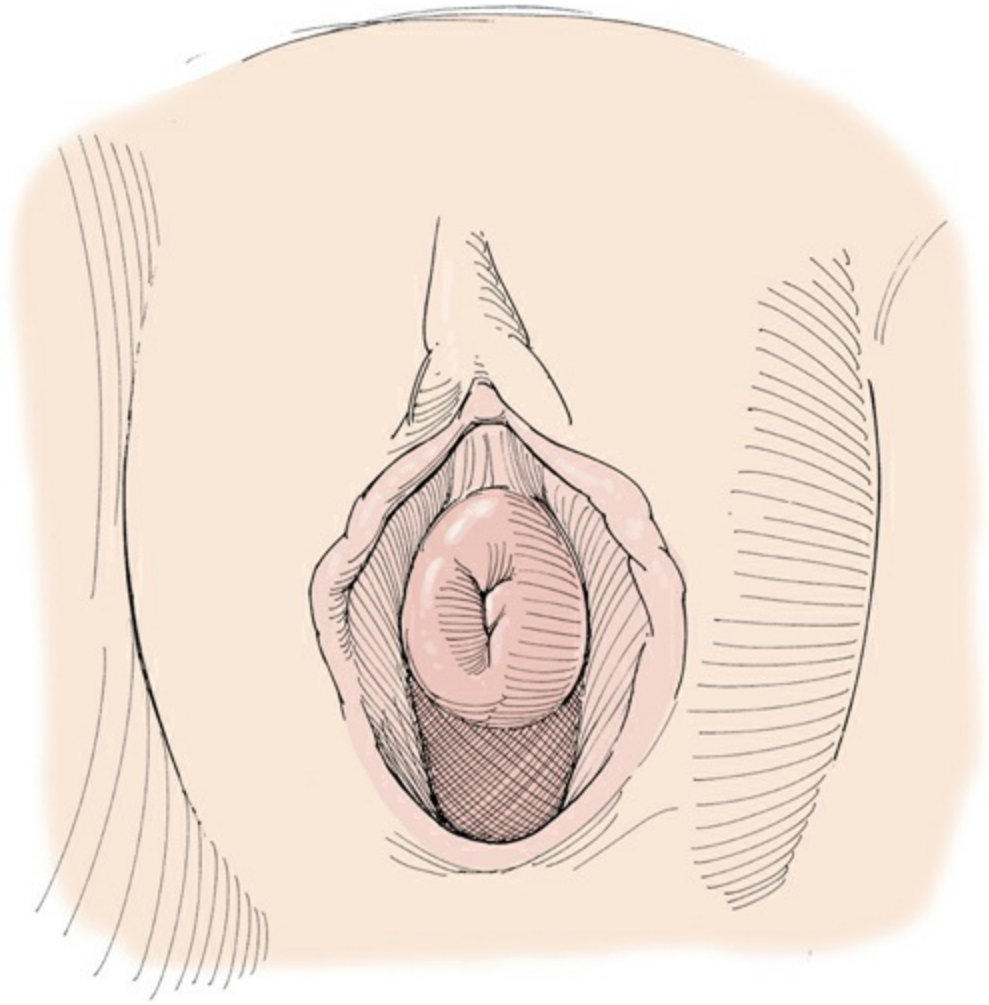

Fig. 30-3 Urethral prolapse.

D. Introital Cysts

Cysts in the introitus in children are usually paraurethral cysts, Gartner's duct cysts, or prolapsed ureterocele.

Paraurethral cysts are dilations of paraurethral glands. These cysts displace the meatus. In the newborn period, paraurethral cysts often resolve with observation. Occasionally, drainage with a small incision or needle may be needed.

Gartner's duct cysts arise from remnants of the Wolffian ducts. They occur along the anterolateral vaginal wall, typically are benign, and often resolve on their own.

There is an association between Gartner's duct cysts and ectopic ureters to vagina due to embryologic origin of Gartner's duct cysts. If there is a cyst seen along anterolateral wall of vagina in an infant or child, evaluation with a renal ultrasound for ectopic ureter to that cyst should be considered.

A prolapsed ureterocele may appear as a pinkish to purple cystic structure in the introitus that can be quite large. They are usually associated with an upper pole of a duplicated kidney and diagnosis is suggested by renal/bladder ultrasound.

E. **Continuous Incontinence and Ectopic Ureter**

In females, an ectopic ureter can insert distally to the urethral sphincter and lead to urinary incontinence (see Chapter 14 and Fig. 14-4). As mentioned above, ectopic ureters to the vagina are thought to be from ectopic ureters to a Gartner's duct cyst that has ruptured into the vagina. Ectopic ureters can also occur near the urethral meatus, on perineum, uterus, and even rarely rectum. Ectopic ureters are often found due to prenatal hydronephrosis or UTIs early in life. However, some females with ectopic ureter will go undiagnosed until after toilet training. They will present with continuous incontinence or wetness. These ectopic ureters that present late are usually from the upper pole of a duplicated kidney. This upper pole may be atrophic and can be missed on renal ultrasound. A high index of suspicion is needed for diagnosis. Magnetic resonance (MR) urograms can be helpful for diagnosis or even an examination under anesthesia. Upper pole heminephrectomy or upper to lower pole ureteroureterostomy are the treatments of choice for continuous incontinence.

II. MÜLLERIAN AND VAGINAL ANOMALIES

The müllerian ducts form the fallopian tubes, uterus, and upper part of the vagina. The distal vagina is formed from the

urogenital sinus. Several types of obstruction, fusion, or duplication anomalies can present in infancy or childhood (Fig. 30-4).

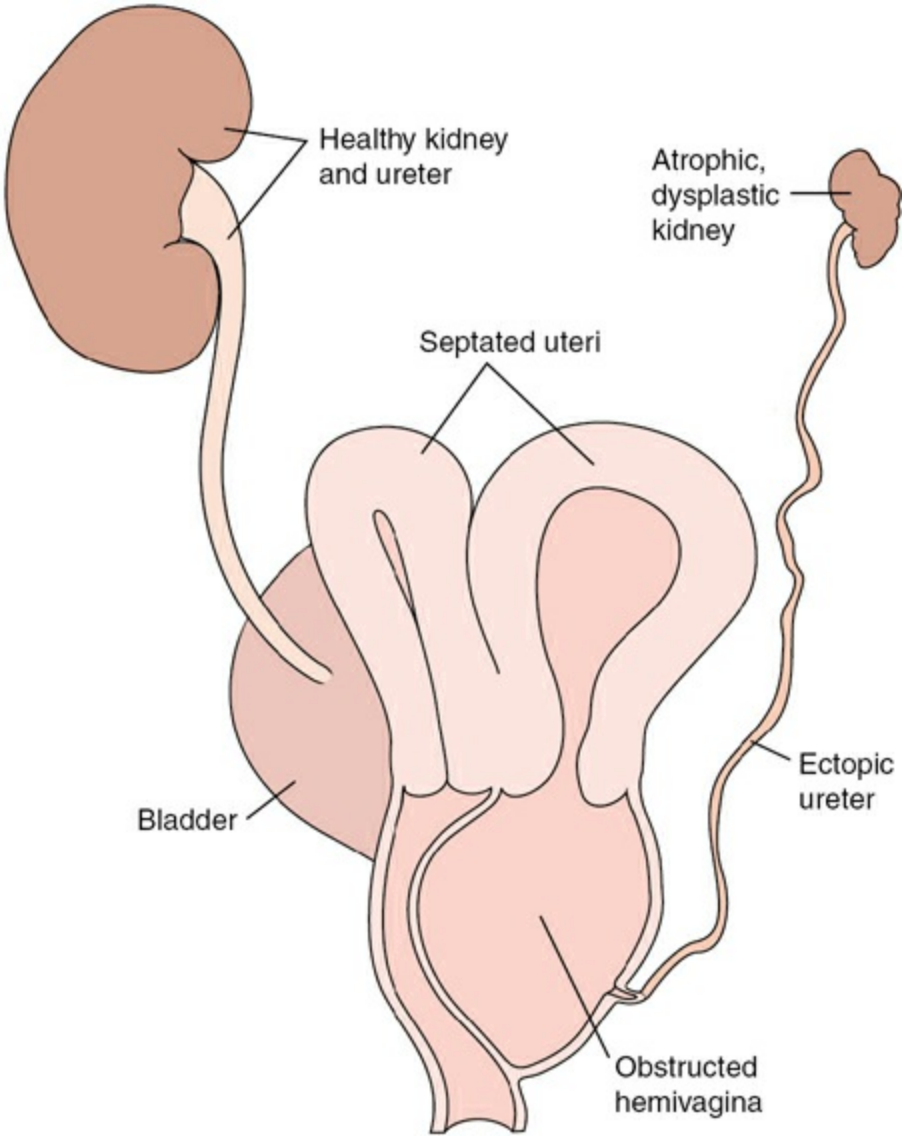

Fig. 30-4 Schematic representation of obstructed hemivagina ipsilateral renal anomalies (OHVIRA) syndrome with an ipsilateral atrophic and dysplastic kidney with ectopic ureter to obstructed hemivagina. The atrophic and dysplastic kidney may be in an ectopic position.

A. Transverse Vaginal Septum

A transverse vaginal septum is thought to be due to a failure of complete canalization of the vagina and occurs in less than 1 per 50,000 females. Transverse vaginal

septa are usually in the mid- to upper vagina and are usually less than 1 cm thick. Patients typically present around puberty with amenorrhea and cyclic abdominal pain due to vaginal obstruction but may present earlier in life. Ultrasound and magnetic resonance imaging (MRI) show a dilated upper vagina and uterus and are useful for diagnosis. Various surgical incisions or excisions for vaginal septa have been described, but all have risk of vaginal stenosis.

B. **Distal Vaginal Atresia**

Vaginal atresia occurs when the urogenital sinus fails to form the distal vagina. This condition is very rare and patients typically present around puberty with cyclic abdominal pain and amenorrhea. MRI and ultrasound are useful for diagnosis. Surgical treatment involves pulling the upper vagina (which is often dilated) to introitus.

C. **Vaginal Agenesis**

Vaginal agenesis occurs when the müllerian ducts fail to form the upper vagina. This condition is also known as Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome and occurs in 1 out of 5,000 female births. There is usually associated agenesis or dysplasia of the uterus and fallopian tubes as well but rarely a functional uterus may be present. Renal anomalies such as renal dysplasia and ectopic ureter may be present as well. Treatment usually involves some type of vaginal replacement either by dilation of distal vagina or by surgical replacement.

D. **Duplication Anomalies**

There is a wide spectrum of müllerian and vaginal duplication anomalies from a partially duplicate uterus to a completely duplicated uterus and vagina. As long as the müllerian ducts are not obstructed, these patients usually do not present before puberty. At the time of puberty, females with a duplicated vagina can have difficulty with placement of tampons and excision of the septum between the vaginas can be performed.

E. **Obstructed Hemivagina and Ipsilateral Renal**

Anomalies

The obstructed hemivagina ipsilateral renal anomalies syndrome or OHVIRA syndrome is an interesting congenital anomaly that affects müllerian structures as well as renal structures. In the OHVIRA syndrome, the uterus and vagina are both duplicated. One of the vaginas is obstructed which leads to cystic dilation of that vagina and associated uterus (Fig. 30-4). This can be detected prenatally by ultrasound. The kidney that is ipsilateral to the obstructed uterus and vagina is usually dysplastic and there is often an ectopic ureter to the obstructed vagina. In infancy, the cystic dilation of the vagina and uterus may resolve with time. If there is persistent dilation of the vagina or symptoms such as UTI, incision of the vaginal septum can be performed in infancy. If there is suspicion for a dysplastic and atrophic kidney with an ectopic ureter, diagnostic laparoscopy with removal of this atrophic kidney should be performed. These dysplastic and atrophic kidneys are often located ectopically in the pelvis. If a child with known OHVIRA syndrome is not treated as an infant, they should have excision of vaginal septum around the time of puberty. In adolescents who present with cyclic abdominal pain, cystic structure in pelvis, and apparent ipsilateral renal agenesis, OHVIRA syndrome should be highly suspected and excision of vaginal septum should be performed. The ipsilateral kidney can be removed if continuous incontinence or wetness occurs after excision of vaginal septum.

III. OVARIAN MASSES

Ovarian masses are uncommon in childhood and adolescence and pediatric urologists should be familiar with the types of ovarian masses and basic management. Around 70% to 80% of ovarian masses in childhood are benign and, given the concern about future fertility in this population, ovary-sparing surgery is the preferred approach when appropriate.

Patients with ovarian masses in childhood most commonly present with symptoms such as abdominal pain and/or abdominal mass. Constitutional symptoms such as malaise, nausea, poor appetite, or weight loss can be seen as well as symptoms from local extent of tumor such as urinary frequency or constipation. If the tumor is hormonally active, precocious puberty or virilization can be seen.

Imaging with transabdominal ultrasound is usually obtained first followed by CT or MRI. Several labs should be obtained when there is an ovarian mass, including α-fetoprotein (AFP), beta-human chorionic gonadotropin (β-hCG), lactate dehydrogenase (LDH), cancer antigen 125 (CA-125), and inhibin. If there is concern for hormonally active tumor, estrogen and testosterone levels should be obtained.

The different categories of primary ovarian masses are germ cell tumors, sex cord–stromal tumors, and epithelial tumors.

A. **Germ Cell Tumors**

Ovarian germ cell tumors include mature cystic teratoma (dermoid cyst), immature teratoma, yolk sac tumor, choriocarcinoma, embryonal carcinoma, dysgerminoma, and gonadoblastoma. All germ cell tumors are considered malignant except for mature teratoma.

Mature cystic teratomas (also called dermoid cysts) are the most common germ cell ovarian tumor in childhood and can be quite large at presentation. Typical imaging appearance is that of a cyst with a focal solid area inside the cyst called a Rokitansky nodule. AFP levels or other labs are not elevated and pathology shows well-differentiated tissue from more than one germ cell layer. Treatment is removal of cyst and this is usually curative.

All other types of ovarian germ cell tumors often have elevated tumor markers (AFP, β-hCG) and are treated by removal of ipsilateral salpingo-oophorectomy followed by

additional staging surgery and chemotherapy if necessary.

B. **Sex Cord–Stromal Tumors**

Sex cord–stromal tumors include malignant types such as juvenile granulosa cell tumors and Sertoli–Leydig tumor, and rare benign tumors such as thecoma and fibroma.

Juvenile granulosa cell tumors (JGCT) often present with precocious puberty due to estradiol secretion by tumor. Corresponding luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels are low. Most JGCT are localized and can be treated by removal of ipsilateral salpingo-oophorectomy. Sertoli–Leydig cell tumors are very rare and patients typically present with signs of androgen excess. Most cases are unilateral and treated with ipsilateral salpingo-oophorectomy.

C. **Epithelial Tumors**

Epithelial tumors include the benign tumor cystadenoma and malignant cystadenocarcinoma and adenocarcinoma. Fortunately in childhood and adolescence, most epithelial tumors are benign cystadenomas. These can present with abdominal pain and can be quite large. If cystadenoma is suspected, surgical removal of the cystadenoma with preservation of the remaining ovary is the approach of choice. At the time of surgery, peritoneal washings and inspection of peritoneum, with biopsy as needed, is performed.

Malignant ovarian cystadenocarcinoma and adenocarcinoma are rare in childhood. CA-125 is usually elevated. Treatment involves ipsilateral oophorectomy, pelvic wash, and biopsy of any suspicious area in the peritoneal cavity or lymph nodes. Further chemotherapy and surgery may be needed depending on the stage of malignancy.

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31 Adolescent Urology: Sexually Transmitted Infections

Bruce J. Schlomer

SEXUALLY TRANSMITTED DISEASES

Sexually transmitted diseases (STDs) do not always present to the pediatric urologist. However, pediatric urologists should be aware of the various types of presentations, differential diagnoses, diagnostic methods, and treatments for STDs. In addition, some STD diagnoses should prompt testing for more STDs and some are required to be reported to public health departments. For most STD diagnoses it is recommended that all sexual partners within the last 60 days be checked and that sexual activity be avoided while symptomatic and until 7 days after treatment is completed.

Herein, we will review the types of STDs based on common types of patient presentations. Treatment, diagnostic testing, and whether reporting to the public health department is necessary will be presented in tabular form based on the most recent Centers for Disease Control (CDC) recommendations. Reviewing the CDC guidelines at the time of any STD diagnoses is recommended.

I. URETHRITIS

Urethritis symptoms include dysuria and mucopurulent or purulent urethral discharge. STDs are typically classified as gonococcal urethritis (GU) caused by *Neisseria gonorrhoeae*

and nongonococcal urethritis (NGU) which can be caused by various other organisms. *Chlamydia trachomatis* causes many cases of NGU along with other organisms such as *Mycoplasma genitalium*, *Trichomonas vaginalis*, herpes simplex virus, and adenoviruses. In addition, it is common that no pathogen is identified in NGU.

Urethritis diagnosis is currently made using nucleic acid amplification tests (NAATs) looking for *N. gonorrhoeae* and *C. trachomatis* in voided urine. A urine analysis should be obtained as well to evaluate for urethral inflammation. Culture of urethral swab can also be done but it has lower sensitivity and is not recommended if NAATs are available. Treatment of GU involves treatment for *N. gonorrhoeae* and possible *C. trachomatis*. Treatment of NGU involves treatment only for likely cause of NGU, typically *C. trachomatis*.

II. EPIDIDYMITIS

Epididymitis in men less than 35 years of age is caused by similar organisms to those that cause urethritis with *N. gonorrhoeae* and *C. trachomatis* being the most common. For men who practice insertive anal intercourse, treatment should cover enteric organisms also. Symptoms include pain, swelling, inflammation of epididymis and sometimes testis as well. Urethritis may be present and epididymal abscess can occur. A scrotal ultrasound is usually obtained to rule out testis torsion/abscess. Urinalysis (UA), urine culture, and NAAT should be used for diagnosis. In men who are likely to have STDs (less than 35 and epididymitis), treatment for both *N. gonorrhoeae* and *C. trachomatis* is given. For men who practice insertive anal intercourse, treatment for enteric organisms is given as well (Table 31-1).

TABLE Diagnosis and Management of Sexually Transmitted

31-1 Diseases

Diagnosis	Preferred Diagnostic Tests	Preferred Treatment	Report Health Depar
Urethritis			
Neisseria gonorrhoeae	UA NAAT	Ceftriaxone 250 mg intravenously once and azithromycin 1 g orally once	Yes
Chlamydia trachomatis	UA NAAT	Azithromycin 1 g orally once	Yes
Epididymitis			
Age under 35 years and likely due to *N. gonorrhoeae* and *C. trachomatis*	UA NAAT Urine culture	Ceftriaxone 250 mg intravenously once and doxycycline 100 mg orally twice a day for 10 days	Yes
Most likely due to STI and enteric organisms (insertive anal intercourse)	UA NAAT Urine culture	Ceftriaxone 250 mg intravenously once and levofloxacin 500 mg daily for 10 days	Yes
Cervicitis			
N. gonorrhoeae	UA NAAT	Ceftriaxone 250 mg intravenously once and azithromycin 1	Yes

		g orally once	
C. trachomatis	UA NAAT	Azithromycin 1 g orally once	Yes
Trichomoniasis vaginalis	NAAT, APTIMA, OSOM, or Affirm VP III assay	Metronidazole 2 g orally once or tinidazole 2 g orally once	No
Genital ulcers			
Herpes	PCR for HSV1 and HSV2	Acyclovir 400 mg orally 3 times a day for 7 to10 days or valacyclovir 1 g orally twice a day for 7 to 10 days	No
Syphilis	Darkfield microscopy for primary; nontreponemal and treponemal for screening and later stages	Benzathine penicillin G 2.4 million units intramuscularly once for primary, secondary, and early latent Benzathine penicillin G 2.4 million units intramuscularly every week for 3 weeks for latent, tertiary no neuro Aqueous crystalline penicillin G 3 to 4 million	Yes

		units intravenously every 4 hours for 10 to 14 days for neurosyphilis	
Chancroid	Culture of *H. ducreyi* on special medium, PCR if available	Azithromycin 1 g orally once or ceftriaxone 250 mg intramuscularly once or ciprofloxacin 500 mg twice a day for 3 days	Yes
Granuloma inguinale	Microscopy with Donovan bodies	Azithromycin 1 g orally every week for 3 weeks and until all lesions healed	No
Lymphogranuloma venereum	See text	Doxycycline 100 mg orally twice a day for 21 days	No

III. CERVICITIS

Cervicitis is characterized by purulent or mucopurulent discharge from the cervix and friable cervical mucosa. Cervicitis may be asymptomatic or present with vaginal discharge or bleeding after intercourse. Cervicitis can be caused by *N. gonorrhoeae* and *C. trachomatis*. NAAT testing should be obtained on vaginal, cervical, or urine samples. *Trichomoniasis vaginalis* can also cause cervicitis and should be tested for using one of several Food and Drug Administration– (FDA-) approved assays that are highly

sensitive and specific, including NAAT. The older method of microscopic evaluation of a wet preparation of genital secretions has poor sensitivity. Therefore, it can still be used to diagnose *T. vaginalis* but cannot rule it out.

IV. GENITAL ULCERS

Genital ulcers from an STD are most commonly caused by genital herpes or syphilis. Other STDs to be aware of that cause genital ulcers include chancroid, granuloma inguinale, and lymphogranuloma venereum. More than one cause can be present in a genital ulcer. The diagnosis can often be made on history and physical examination alone. All patients with genital ulcers from presumed STD should be tested for herpes and syphilis. Other causes of genital ulcers should be tested for if a known outbreak is present in the area or clinical suspicion exists. See Table 31-2 for description of the clinical presentations of genital ulcer diseases.

TABLE 31-2 Differentiating STDs That Cause Genital Ulcers

Genital Ulcer Disease	Differentiating Signs and Symptoms
Herpes	Clusters of painful papules and vesicles about 1 week after sexual intercourse. May have prodrome of fever, malaise, headache, muscle aches. Initial infection with lesions can last a few weeks. Recurrences can occur but are usually milder.
Syphilis	Typically painless ulcer called a chancre occurs 2–3 weeks after infection.

	Painless lymphadenopathy is common. Chancre heals within 3–6 weeks. Secondary syphilis: rash on palms and soles, constitutional symptoms several months after primary infection. Tertiary syphilis: involvement of brain/spinal cord or cardiovascular system, gummatous lesions. Latent syphilis: asymptomatic, picked up by screening when diagnosed with other STDs.
Chancroid	Painful genital ulcer or ulcers with suppurative inguinal lymphadenopathy 3–10 days after infection. Inguinal lymphadenopathy is typically very tender and may progress to bubo formation. Typically associated with outbreaks or travel to endemic areas such as Africa or Asia.
Granuloma inguinale	Very rare in the United States. Slowly progressing genital ulcers without inguinal lymphadenopathy. “Beefy red” ulcers that are friable.
Lymphogranuloma venereum	A small papule or ulcer occurs but often goes unnoticed. Patients present with tender inguinal lymphadenopathy. Those who practice insertive anal intercourse can present with proctocolitis. Outbreaks can occur in men who have sex with men.

Herpes is very common with approximately 50 million people in the United States having infection with most being undiagnosed and many asymptomatic. Genital herpes is usually caused by herpes simplex virus-2 (HSV2) but can also be caused by herpes simplex virus-1 (HSV1). Patients with herpes should be informed that recurrent episodes may occur and that HSV viral shedding can occur when asymptomatic. They should be advised about the importance of informing current and future sexual partners and the increased likelihood of HIV transmission during outbreak of ulcers. If herpes leads to recurrent outbreaks, suppressive therapy can be given such as acyclovir 400 mg by mouth twice a day or valacyclovir 1 g by mouth daily.

Syphilis is caused by *Treponema pallidum*. Primary syphilis is the most common type that would present to a urologist and is characterized usually by a painless ulcer (chancre) at the infection site. The chancre typically resolves after 3 to 6 weeks. Secondary syphilis appears a few months after primary syphilis and is characterized by rashes on scalp, palms of hands, and soles of feet as constitutional symptoms of fever and malaise. The rash is maculopapular and wartlike lesions can occur. After secondary syphilis resolves, the infection becomes latent syphilis and is asymptomatic. Tertiary syphilis includes numerous late manifestations of syphilis including neurosyphilis and cardiovascular syphilis. Exudate or tissue from the chancre can be evaluated using darkfield microscopy to detect *T. pallidum* and is the definitive method for diagnosing early primary syphilis. A nontreponemal test (either Venereal Disease Research Laboratory [VDRL] test or rapid plasma reagin [RPR] test) and a treponemal test (fluorescent treponemal antibody absorption [FTA-ABS], Treponema pallidum particle agglutination [TP-PA] assay, or other assays) should also be

sent for when testing for primary syphilis, when screening for syphilis due to the presence of other STDs, or when testing for later stages of syphilis. Syphilis can be hard to diagnose, but the treatment is usually Penicillin G as the preferred drug. The length of treatment depends on the stage of the disease (Table 31-1).

Chancroid caused by *Haemophilus ducreyi* is relatively uncommon in the United States and is mainly associated with outbreaks. The diagnosis should be suspected if there is an outbreak in the area and patient presents with painful genital ulcer with suppurative inguinal lymphadenopathy. Diagnosis can be confirmed with growth of *H. ducreyi* on special culture media, but sensitivity is relatively low. Polymerase chain reaction (PCR) tests are available in some centers.

Granuloma inguinale, or donovanosis, is caused by *Klebsiella granulomatis*. It is rare in the United States. *K. granulomatis* is hard to culture and diagnosis is confirmed by visualization on microscopy of Donovan bodies, which are rod- to oval-shaped bacteria seen in the cytoplasm of white blood cells that stain purple with Wright's stain. Inguinal adenopathy is usually not seen and ulcers are painless.

Lymphogranuloma venereum is caused by *C. trachomatis* serovars L1, L2, and L3. A self-limited genital ulcer may be found but often patients present with tender inguinal lymphadenopathy. Rectal exposure can lead to proctocolitis symptoms as well. Outbreaks among groups at risk can occur such as men who have sex with men (MSM). Diagnosis is often based on clinical suspicion and ruling out other causes of proctocolitis. NAAT testing can be used but is not FDA-approved for the diagnosis of lymphogranuloma venereum. Other tests such as culture, immunofluorescence, and PCR testing have been used.

RECOMMENDED READING

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32 Transitional Urology

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I. INTRODUCTION

Children are born with a wide range of congenital anomalies. As many of these children are living longer due to advances in medical care, they are growing into adulthood with their problems managed, but not cured. These children become adults in need of complex medical and urologic care. As these patients age, they often continue to have active and changing urologic issues that require ongoing care for their entire lives. They also develop nonurologic problems and conditions that are much more familiar to adult providers. Additionally, anesthesia providers at adult hospitals are often better equipped to deal with specific comorbid conditions and adult specific physiology. Even when adult urologists are attuned to these patients' needs and have expertise in their specific reconstructive needs, they often do not have the same multidisciplinary support systems that exist in pediatric hospitals.

To date, there is no single definition of transitional urology or congenitalism. In general, the field strives to effectively and seamlessly transition patients with complex congenital or childhood urologic issues into the adult world. Given the complex problems these patients face, they have often established long-standing relationships with their care providers in the pediatric world. As pediatric urologists tend to be very invested in the care of these patients, they have a

strong desire to identify providers who will maintain this same standard of care going forward. The transitional urologist strives to effectively fill this niche.

A. Challenges

Transitional care certainly provides challenges for both patients and providers. Patients are often reluctant to transfer care away from providers and institutions that they have bonded with from a young age and who know them well. Adult urologists often feel undertrained to manage the problems facing these complex patients. Additionally, initial appointments can be daunting for both patient and provider alike, as records from multiple previous surgeries, hospitalizations, and treatments can be difficult to obtain and time-consuming to review.

A large commitment is necessary to understand the unique history, anatomy, and social situation of these patients. In a health-care climate that is often driven by financial considerations, current reimbursement schemes do not often incentivize providers to undertake these types of patients or visits. Moreover, staff at adult urology clinics are often unfamiliar with many pediatric urologic conditions. Front desk personnel, nurses, and advance practice providers require education about the specific needs of this patient population to feel comfortable addressing the issues, interacting with their families, and participating in the care.

The development of multidisciplinary treatment groups is not an easy task, and requires commitment from a wide range of providers. Even in pediatric centers this is often difficult to come by, and becomes a nearly unattainable challenge in the busy adult world. Identifying primary care providers and pertinent specialists with an interest and expertise in transitional care becomes vital to successfully moving the care

of these complex patients into the adult setting.

While this all may seem daunting, for those providers who focus on transitional care, helping these patients obtain excellent care into adulthood makes these struggles worthwhile.

B. Research

Research and clinical data in the field has been sparse but steadily increasing. Not surprisingly, most studies to date have been limited by retrospective data collection, small patient populations, and limited long-term follow-up. Little collaboration has been established as yet between pediatric and adult departments or even among institutions. As the field continues to grow, there will undoubtedly be more room to advance the care we provide for these patients with better data collection and research to guide better practice. Moreover, better quantifying of long-term outcomes for these patients will be likely to allow us to improve our care of these patients from the earliest stages.

C. Conditions

Many patients suffer from conditions that begin in childhood and remain present well into adulthood, such as varicoceles, stone disease, and urinary tract infections (Table 32-1). Most of these can be more seamlessly transitioned to adult care as these fit into the scope of practice of many adult urologists. The infertility specialist or the stone specialist would also have the capacity of taking care of even challenging patients with these conditions who are transferring care from a pediatric to adult provider. The key areas for transitional urology are those conditions that require specialized care and expertise not readily available to the adult urologist or that require a far more multidisciplinary approach. Thus we will limit the scope

of this chapter to those.

In general, many congenital anomalies that persist into adulthood lead to challenges with fertility, sexuality, quality of life, and independence. As children grow, puberty and adolescence lead to change and growth both physically, psychologically, and physiologically. It is critical to adapt to these changes with the patients, and guide them to the right avenues for ongoing care. Some patients face specific challenges of maintenance of complex reconstructions, such as complications of stomas, strictures of reconstructed urethra and vaginas and ureters, or bladder outlet obstruction. Other patients face ongoing continence concerns of both bowel and bladder. Additionally, standard health-care prevention becomes critical in patients predisposed to conditions such as cardiovascular disease, stone disease, renal failure, and cancer.

TABLE 32-1 Transition Care: Congenitalism

Recommended management by adult urologist with area specialization:
varicoceles, stone disease, and urinary tract infections
Recommended management by transition care specialist with expertise in adult and pediatric urology:
exstrophy, hypospadias, posterior urethral valves, spina bifida, disorders of sexual development, and childhood urologic cancers

D. Timing of Transition

The optimal time to begin transitioning patients to adult providers has yet to be defined and will likely vary based on a number of factors. That said, initial introductions of patient and their family to the adult provider in a familiar setting at a relatively early age with the longtime provider present may be of benefit in easing the transition. Reassuring patients and

families that a plan is in place for their ongoing care seems to be of tremendous value.

II. EXSTROPHY

Bladder exstrophy (BE) is a rare congenital anomaly that occurs in 1 per 50,000 newborns, and exists on a spectrum from isolated epispadias to cloacal exstrophy, which is even rarer. The care of bladder exstrophy is a challenge even to the trained pediatric urologist who on average may see three patients per year in “high volume” centers. While the initial surgical reconstruction and management of early bladder development is challenging and there is little concrete data to guide each step, there is even less guidance of management as these children grow into adulthood. Patients with bladder exstrophy have a lifetime of concerns with continence, urinary tract infections, fertility, sexual function, and cosmesis, and these are challenges for almost every patient and any urologist, adult and pediatric alike.

A. Continence

Long-term continence rates in patients with exstrophy are variable, and the data available may not be completely applicable to guide our current generation of exstrophy patients since closure patterns have changed. Most patients with augmentation and catheterizable channels or complete urinary diversion will be dry, but even some of these patients will leak via the stoma or have stress incontinence. A small minority are dry with their initial reconstruction alone. It is important to remember however that patients who have achieved continence with reconstruction alone or with bladder neck reconstruction may seemingly void well for a while, but are still at risk for incomplete emptying and its sequellae, as well as long-term bladder decompensation as they are

ultimately voiding against a fixed outlet resistance. This low level of obstruction may be well tolerated initially, but can lead to decompensation of the upper tracts so these patients have to be monitored throughout life.

B. Urinary Tract Infections (UTIs)

Patients with bladder exstrophy who undergo reconstruction with augmentation or urinary diversion are especially at risk for urinary tract infections (UTIs). Even those who were reconstructed primarily may be at risk for infections due to incomplete emptying. In addition men with a history of bladder exstrophy may void at higher pressures, Valsalva void, or have an element of obstruction which predisposes them to epididymitis. Thus these patients have to be carefully assessed when they present with recurrent UTIs or epididymitis to ensure that their upper tracts are preserved and to rule out significant obstruction.

C. Cosmesis

The external appearance of men with bladder exstrophy is notable not just for the penile shape, but also for the hair distribution. Pubic hair grows on either side of the midline, but not in the area of the diastasis itself. This can at times be bothersome to patients, and can be corrected by rotating hair-bearing flaps of skin medially to cover the defect.

One of the greatest concerns for men with bladder exstrophy is penile length and dorsal chordee. While the dorsal chordee can be corrected if there is a specific functional problem, there is little that can be done about penile length. There are reports of radial free-flap phalloplasty with inflatable penile prosthesis, but this is not a widely performed procedure and is fraught with complications.

The perineum of women with bladder exstrophy is

displaced anteriorly, and the vagina is positioned almost parallel to the floor while standing. The vagina also tends to be shorter than normal. The labia are small and are not fused to form a fourchette. The clitoris is bifid, which persists even after reconstruction. While some of this reconstruction can be done in infancy during the initial repair, any clitoral surgery is done with caution and even reconstruction in adulthood can lead to decreased sensation.

D. Fertility

The testes in boys with bladder exstrophy are anatomically normal; however there is an increased association with undescended testes, which according to some reports occur in up to 23% of boys. There is not good data on the semen quality in men with a history of bladder exstrophy. It has been thought that about one-third to one-half of men with BE can achieve paternity, but this may require assisted reproductive techniques. Infertility can be due to leukospermia or scarring of the seminiferous tubules due to inflammation, or impairment of transit of sperm due to injury of the vas or ejaculatory ducts, or impaired ability to transmit sperm to the partner’s cervix.

In women with BE, the ovaries and uterus are normal and uninvolved. However the cervix is positioned low and close to the introitus and there is deficiency in the pelvic floor with the pelvic floor musculature located posteriorly, thus providing less support to the vagina and bladder. This lack of support predisposes women to prolapse. In a Spanish cohort, 31% of women with repaired exstrophy had genital prolapse, and in some series, up to 50% of women with exstrophy developed prolapse. Genital prolapse was more common after pregnancy, but did occur in nulliparous women as well.

Women with BE can carry successful pregnancies. They

should be counseled on the increased risk of UTIs during pregnancy and the likely need for Cesarean section for delivery. In patients with a catheterizable stoma, the pregnancy can lead to alterations in the anatomy of the channel, leading to difficulty with draining. In 2015, the Seattle group published its longitudinal review of a total of 12 women with history of bladder exstrophy complex who attempted pregnancy. Of these 12 women, there were totally 22 pregnancies (20 in bladder exstrophy and 2 in cloacal exstrophy), with a total of 14 live births, 4 spontaneous abortions, and 4 terminations. The majority of these patients had bladder augmentations and some had catheterizable channels or performed clean intermittent catheterization (CIC) per urethra. The live births were all delivered by Caesarian section via a vertical paramedian incision rather than the standard Pfannenstiel incision.

E. Sexual Function

While the anatomy of bladder exstrophy should not affect tumescence, men with bladder exstrophy do have a higher rate of erectile dysfunction (ED) based on the International Index of Erectile Function score, with 58% having a score of 15 or less compared to 23% in controls. The areas of dysfunction were in the ability to maintain an erection and penetration, but not frequency and rigidity of erections.

The evaluation of erectile dysfunction in patients with bladder exstrophy is no different than in men without bladder exstrophy. Standard medications can be trialled. However, the physician must remember that each each corpus cavernosum is separate with no cross circulation, and so any intracorporeal injections have to be administered into each side separately.

Dyspareunia is a significant problem for women with bladder exstrophy, occurring in 42% to 50% of women in

some series. This is in part caused by the anatomy of a narrow introitus. Sexual desire seems to be normal for women with BE, and females have been reported to masturbate regularly and achieve orgasms in 50% to 67% respectively. There is no good data on the specifics of sexual function. Overall, about 79% of women with bladder exstrophy report being sexually active, although this was from only a small cohort of women with bladder exstrophy, so again reporting bias is critical. In another small report of classic bladder exstrophy, 7 women were satisfied with their sexual lives and 4 were not, 3 due to cosmesis and 1 due to dyspareunia.

F. Quality of Life

There is scarce literature on the quality of life (QoL) for patients who have grown up with BE, although this has become an important topic which is being studied currently. Moreover, as the repairs have changed, children will grow up with different experiences, so the prospective collection of QoL data is critical. A history of bladder exstrophy can have effects on sexual function as well as on continence, which affects mental health and anxiety disorders. Selection bias is an inherent flaw in all QoL research. However, until routine prospective questionnaires are filled out at each follow-up visit, retrospective reports are the only available data. In one recent retrospective questionnaire study, researchers found that bladder exstrophy patients scored equal to their peers in all things except physical functioning, mental health, and emotional role. On a positive side, this study was in concordance with previous findings that patients with bladder exstrophy tend to be above the peer average in graduation from high school and future pursuit of higher degrees.

III. HYPOSPADIAS

Given how commonly hypospadias is encountered by the pediatric urologist (1 per 200 to 300 live births, and likely rising in the age of in vitro fertilization [IVF]), it is not surprising that many adult men have been treated for this condition earlier in life. Interestingly, a fair number of men likely have no knowledge that they have the condition, whether they had surgical correction in the past or not. Accordingly, follow-up for these patients is often poor, limiting our true understanding of how many of these patients do as young men and adults. While undoubtedly many of these men have done well from both a urinary and sexual standpoint, a subset of them will require ongoing care into adulthood. The incidence of late failures is currently unknown, as these presumably derive from a myriad of patient-specific and technical factors from the initial repair.

A. Cosmesis

Penile appearance is a concern for many men as they reach adulthood, with men with hypospadias being no exception. Primary sources of dissatisfaction for men with hypospadias include penile size and residual chordee. Assessing patient satisfaction with penile cosmesis has been somewhat challenging, but several objective methods have been developed for this patient population. The Hypospadias Objective Scoring Evaluation and Pediatric Penile Perception Score have both been used to quantify penile appearance objectively to allow comparison. Generally, satisfaction rates reported by patients with their cosmesis after hypospadias repair is substantially lower than those reported by parents or surgeons.

B. Urethral Strictures and Urinary Issues

As hypospadias is characterized by a lack of normal distal

corpus spongiosum and therefore by definition, an abnormal blood supply to the urethra, urethral stricture disease is significantly more common in the hypospadias population. For the same reasons, these strictures are also more challenging to address than the more common post-traumatic strictures often encountered in adulthood. Additionally, after multiple previous operations, these patients also seem to have a higher rate of lichen sclerosus development creating additional challenges for reconstruction. Fortunately, many adult reconstructive urologists are quite familiar with the management of strictures in the hypospadias population. Again, these strictures tend to be relatively challenging to repair given the congenital dearth of corpus spongiosum tissue coupled with the decrement in tissue vascularity and quality secondary to multiple previous attempts at repair.

Even with successful repair, many patients with hypospadias will continue to have abnormalities of their urinary stream. Without a natural fossa navicularis, the urinary stream does not spiral naturally, altering the flow dynamics and making the stream less consistent and less straight. Patients are more likely to complain of urinary spraying or splaying after hypospadias repair, even if the urethra appears widely patent on imaging or cystoscopy. As the tip of the urethral meatus may not be brought out to the tip of the glans, many of these patients continue to have a mild hypospadias, leading to a downward deflection of their stream.

Additionally the use of flaps and grafts in hypospadias repair leaves the urethra without the natural elasticity of the normal urothelium. This leads to alterations in the urinary flow curve, and in some men, a slightly diminished, albeit not pathologically so, flow rate. Urine may also pool slightly in these areas, leading to postvoid dribbling with the occasional need to “milk” the urethra to expel the end of the urinary

stream.

C. Sexual Health

Residual chordee after hypospadias repair is often manifested at puberty. This will often need to be aggressively managed in addition to any stricture disease to allow for successful outcomes. Currently, there is little in the literature regarding long-term outcomes in curvature or erectile quality in patients undergoing different types of chordee repairs in childhood. While data is limited, there does not seem to be an increase in erectile dysfunction in adults with hypospadias, regardless of whether they have undergone repair in the past.

Ejaculatory problems in adulthood can also be a major concern for patients with hypospadias and seem to occur at a higher rate in men with a history of hypospadias. This is not only a concern for men from a sexual health perspective, but also can be important from a fertility standpoint. While this likely occurs secondary to the natural lack of corpus spongiosum in the native or reconstructed urethra or potential development of urethral stricture, other less common causes include pooling of semen in a diverticulum, ejaculatory duct scarring, or retrograde ejaculation, and these etiologies should be considered in this population.

Interestingly, while patients with isolated hypospadias seem to have similar semen parameters compared to men without hypospadias, they do seem to have a decrease in their overall paternity and an increased likelihood to seek fertility services.

D. Repair

Patients with hypospadias-related strictures in adulthood warrant special consideration when it comes to repair. As many of these patients have undergone one or more surgical

procedures previously, tissue planes and vascularity tend to be compromised to various degrees. Portions of the urethra may be significantly scarred, requiring complete replacement. Additionally, complicating factors such as urethrocutaneous fistula or urethral diverticula may be present, further compromising tissue integrity.

Careful preoperative assessment of the local tissue quality and tissue available for grafting or flap creation is essential. Additionally, preoperative assessment with imaging, such as retrograde urethrography and/or voiding cystoscopy urethrography as well as endoscopic evaluation (if possible), is necessary to provide accurate staging. While often challenging, obtaining any previous operative reports can be immensely helpful when planning reoperative procedures.

In select patients with adequate available healthy tissue, redo repairs can be performed in a single stage using standard reconstructive techniques. If grafts, such as buccal mucosa are used as a substitution material, care must be taken to assure that adequate host bed vascularity is available to allow for graft take. Alternatively if a penile skin flap is used for tissue replacement, adequate healthy local penile skin must be available to mobilize. Additional healthy vascularized tissue must also be mobilized for coverage of the urethroplasty site to minimize the risk of fistulization. When any of these are in considerations are in doubt, multistage repairs may be utilized to transfer healthy tissue and assess for healing and take at each step. As with other types of repairs, tubularized graft repairs generally have lower success rates than substitution onlay or inlay repairs and should be avoided. As with other types of repairs, tubularized grafts generally do worse than onlay or inlay repairs. Standard operative techniques such as TIP repairs are often less effective in the redo patient. Urethral dilation or direct vision internal urethrotomy (DVIU) for

hypospadias strictures within the penile urethra tends to have abysmal success rates.

More often, reoperative hypospadias cases in the adult population necessitate a staged approach to adequately correct residual chordee, bring in vascularized tissue to provide a bed for graft take, transfer tissue for urethral reconstruction, recreate the urethral tube, and provide adequate skin coverage. An open and honest discussion about the surgical plan, what can be expected between the various stages, and an understanding that the plan may need to be modified en route is crucial to successful outcomes. For many adult men, fear of undergoing a staged procedure, and the cosmetic changes associated with penile surgery and fear of a decrement in sexual function may lead them to delay care significantly.

For adults with uncorrected hypospadias who request repair, standard techniques such as Thiersch-Duplay repairs or TIP have been shown to be quite effective in the postpubertal population. There does seem to be a higher rate of urethral complications in primary adult hypospadias repairs (10% to 50%) than in similar repairs in children employing standard techniques.

IV. SPINA BIFIDA

Children born with spina bifida are one of the largest populations who will require transition of care as they grow into adulthood. Many pediatric centers have dedicated spina bifida clinics where patients see specialized pediatricians and pediatric nurses, urologists, orthopedists, neurosurgeons, as well as physical therapists and social workers. Unfortunately, these types of clinics do not usually exist in adult hospitals. Even when a urologist can be found who is willing and able to care for these complex patients, it remains a challenge to find all the different specialists to care for these patients.

In this day and age, the majority of patients are managed with clean intermittent catheterization with or without augmentation, and some with vesicostomy. The status of the bladder can change over time, and thus they require monitoring at all ages. These children and adults with neurogenic bladder remain at risk for infections and stones, urethral strictures and bladder cancer, and changes in compliance leading to upper tract deterioration in the long term. Patients who undergo augmentation or diversion with catheterizable channels are also at risk for stenosis or strictures of the channels, augmented perforation, or metabolic abnormalities including metabolic acidosis, vitamin B_{12} deficiency, and bone mineral density abnormalities. In addition to these concerns, continence remains a lifelong struggle for some of these patients.

The management of neurogenic bladder always goes hand in hand with neurogenic bowel. In some centers, this is managed by a dedicated gastrointestinal (GI) team. However, in most, the urologist guides the bowel management, and this does not necessarily end in childhood. The options available for neurogenic bowel management in adults remain the same as in children, with the goal of starting with oral medications, and proceeding in a stepwise manner to rectal suppositories and enemas, retrograde irrigation systems (cone, Peristeen), antegrade enema systems (Malone, Chait tubes), and finally referral for colostomy.

The long-term management of patients with neurogenic bladder (primarily from spina bifida, but also from other bladder pathologies such as posterior urethral valves and bladder exstrophy), involves the evaluation for potential bladder cancer later in life. It has been found that these patients not only have an increased risk of bladder cancer (up to 4.6% versus 2%), but it occurs earlier and at more advanced

stages than the general population. Moreover, it is not just bladder augmentation that predisposes to cancer as previously thought, but also potential inflammation that results from CIC alone, or the immunocompromised state that results after renal transplantation. While the long-term surveillance strategy for these patients is yet to be conclusively determined, it is at least important for these patients to have a urologist to monitor routine labs and urinalysis and proceed to further imaging or cystoscopy when indicated.

V. POSTERIOR URETHRAL VALVES (PUV)

The long-term care of boys with posterior urethral valves (PUV) involves management of continence and bladder emptying, urinary tract infections, and progression to renal failure. The valve bladder is characterized by chronic overdistention that is due to incomplete emptying (both from failure of detrusor function and drainage of dilated upper tracts), polyuria leading to dilation, and decreased bladder sensation. This constellation can often be improved by overnight catheter drainage, with or without daytime CIC.

While a large subset of these patients will progress to *end stage renal disease* (ESRD) early in childhood or adolescence, there is a group who may linger and progress to ESRD only in adulthood. A group from Helsinki looked at a group of 193 patients ranging in age from 6 to 69 years, and found 22.8% (44 patients) progressed to ESRD, but of these 44, 14 (32%) had progression later in life, but no later than 34 years. It is thus crucial to follow these children closely even as they enter adulthood, especially those with history of poorer early presentation, perinatal pneumothorax, bilateral vesicoureteral reflux (VUR), and recurrent UTIs.

In addition to bladder and renal concerns that progress into adulthood, boys with PUV may have persistent voiding

dysfunction, fertility concerns, and sexual function concerns. In yet another survey study, patients with PUV from Spain were assessed, and 16 out of a total of 47 patients were able to be contacted and they returned the questionnaire. In these results, there was a very low incidence of mild incontinence and weak urinary stream, while none reported bladder overactivity. Additionally, only 4 had some degree of erectile dysfunction and ejaculation was normal except for 1 patient on dialysis.

VI. DISORDERS OF SEXUAL DIFFERENTIATION (DSD)

Children with disorders of sexual differentiation (DSD) are followed closely by both urology and endocrinology. In adulthood, this care must continue, along with surveillance for malignancy that can develop in müllerian remnants or gonadal structures. Girls with c*ongenital adrenal hyperplasia* (CAH) are not at higher risk for gonadal malignancy but any DSD with dysgenetic gonads containing a Y-chromosome are at increased risk. Dysgenetic gonads are at high risk for gonadoblastoma.

The incidence of girls born with a persistent cloaca is about 1 per 50,000 live births, and this anomaly occurs along a spectrum. While the immediate management consists of stabilization, decompression of hydrometrocolpos, and bladder drainage, the secondary reconstruction is often the most challenging.

Now that these girls are growing to adulthood, they face problems of obstruction and stenosis of the genital tract. Of one cohort of patients with childhood repair of cloacal anomalies 56% required vaginal reconstruction to facilitate menstruation and satisfactory sexual activity. Moreover this cohort had a high rate of müllerian anomalies that were

identified and managed in an older age group. These patients may require vaginal dilation or complete reconstruction with grafting to enlarge the vaginal lumen.

Anatomic challenges in these patients include the length of the common channel available to make into a urethra and functioning vagina, as well as variable müllerian anomalies including duplicated or obstructed systems. The urethra also may develop stenosis or the bladder may not drain entirely, leading to the need for intermittent catheterization or even continent catheterizable channels to ensure adequate emptying.

Even as reconstructive procedures evolve, it is critical to monitor these patients as they reach menarche and beyond, and as more reach reproductive age, it will be critical to have a unified approach with gynecology as well as urology to offer the optimal management to these women. Additionally, patients who have undergone complete reconstruction with creation of a neovagina are at risk for cancer of that structure, including squamous cell cancers of skin grafts and adenocarcinoma of bowel segments. Thus although rare, any woman who presents with bloody discharge or postcoital bleeding should be evaluated.

Patients with DSD and cloacal anomalies should be aware of difficulties with fertility. Girls may require vaginal dilation or relief of stenosis. Most girls will be fertile, but will likely require Cesarean delivery. Men with DSD may have persistent hypospadias or curvature.

VII. CHILDREN WITH CHILDHOOD CANCERS

With the survival of childhood urologic cancers upward of 90% for Wilms tumors and 80% for rhabdomyosarcoma, these patients will require surveillance as well as management of sequelae from surgery into adulthood. Major surgical

resections that are often required in cases of rhabdomyosarcoma may leave patients with urinary diversions including ureterostomies, ileal conduits, or ileal neobladders, and they remain at risk for stricture, urinary tract dilation, and bowel obstruction at all ages.

Many of these patients will receive chemotherapy and radiation during their treatment, which may lead to end-organ effects such as hypertension and pulmonary disease or even hemorrhagic cystitis. Treatments themselves put these patients at risk for secondary malignancies that require surveillance. Chemotherapy can lead to infertility due to altered spermatic function or hormonal levels, which will require careful counseling and treatment planning as these patients start to form families of their own. Additionally, cisplatin-based chemotherapy can lead to hemorrhagic cystitis and fibrotic changes to the bladder.

All children with a history of childhood urologic cancer should transition to an adult provider who understands their history and their past treatment, and who is able to treat the complications that may arise in the future.

VIII. IMPLICATIONS FOR THE FUTURE

Unlike many patients seen in both pediatric and adult urologic practices, individuals with congenital urologic issues often require a lifelong multidisciplinary approach to ensure optimal management. Coordinating the right team of primary care physicians and specialists to provide care in a seamless manner makes transition of these patients an often daunting prospect, especially if there is no system already in place.

As urologic transitional care is in its infancy, tremendous challenges lie ahead. We must continue to learn from experience to define whether an optimal transition structure exists or whether each patient and family must be approached

on an individualized basis. What works well at one institution may not be ideal for another. Urologists who are willing to gain training and expertise in transitional care must be identified and fostered. Appropriate funding to continue necessary programs for these individuals and to sustain meaningful research efforts must be secured.

Further research on not only outcomes but also on patient-reported quality of life measures will help us improve care for these patients in adulthood, and may allow us to rethink how we approach their management from infancy (or perhaps even earlier). Although designing these studies and collecting the necessary data may be challenging, this surely will allow us to further improve the care of this often-underserved population.

IX. SUMMARY

Successful transition of patients with congenital urologic issues requires a dedicated team of practitioners to coordinate their often complex medical care (Table 32-1). Patients with conditions such as exstrophy, hypospadias, posterior urethral valves, spina bifida, disorders of sexual development, and childhood urologic cancers face a unique set of issues that are often less familiar to many practicing adult urologists. They often require lifelong care to optimize both their urologic and nonurologic conditions. Helping patients to effectively transition their care from pediatric to adult providers should ensure the best possible long-term outcomes both for them as patients and for us as providers. Much work remains to be done to ensure that this can be done successfully for all of these individuals.

RECOMMENDED READING

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33 Pediatric Urology Database

Jeffrey A. Stock

I. INTRAVENOUS FLUID THERAPY

A. Maintenance of Normal Kidney Function

1. Fluid requirements
    a. Method to estimate daily maintenance rate of fluid
        (1) First 10 kg body weight: 100 mL/kg per day
        (2) Second 10 kg body weight: 50 mL/kg per day
        (3) Third 10 kg body weight and beyond: 25 mL/kg per day
        (4) Example 1: A 3-kg infant requires 300 mL fluid per day
        (5) Example 2: A 13-kg child requires 1,150 mL fluid per day (1000 + 150 mL)
        (6) Example 3: A 40-kg adolescent requires 2,000 mL fluid per day (1,000 + 500 + 500 mL)
    b. Method to estimate hourly maintenance rate of fluid
        (1) First 10 kg body weight: 4 mL/kg per hour
        (2) Second 10 kg body weight: 2 mL/kg per hour
        (3) Third 10 kg body weight and beyond: 1 mL/kg per hour
        (4) Example 1: A 3-kg infant requires 12 mL per hour (3 kg × 4 mL/kg/h = 12 mL/h)
        (5) Example 2: A 13-kg child requires 46 mL per hour [(10 kg × 4 mL/kg/h) + (3 kg × 2

mL/kg/h) = 46 mL/h]

(6) Example 3: A 40-kg adolescent requires 80 mL per hour: [(10 kg × 4 mL/kg/h) + (10 kg × 2 mL/kg/h) + (20 kg × 1 mL/kg/h) = 80 mL/h)]

2. Electrolyte requirements
   a. Na^+: 50 mEq/m^2 per day or 3 to 4 mEq/kg per day
   b. K+: 20 mEq/m^2 per day or 2 mEq/kg per day
3. Appropriate solution: The most appropriate solution for routine fluid therapy in postoperative patients is Lactated Ringers (LR).
4. Losses: Losses (e.g., nasogastric suction) must be replaced accurately. Children are best followed up for dehydration by monitoring urine output. If the urine output is between 1 and 2 mL/kg per hour, the appropriate amount of fluid is probably being given.

II. PEDIATRIC UROLOGY FORMULARY

The information provided is not comprehensive. Please consult a more complete reference before using medications with which you are unfamiliar. (Please note that in the "Supplied As" category, the unit quantity in which a drug is supplied is noted in parentheses after the drug concentration; Table 33-1.)

TABLE 33-1 Pediatric Dosages

Drug	Dose	Supplied As
Analgesics		
Acetaminophen (Tylenol)	10–15 mg/kg/dose Q4–6 h PO	Tabs: 160, 325, 500, 650 mg Chewable tabs:

		mg Drops: 80 mg/0 mL Elixir: 120, 130 160, 325 mg mL Caplets: 160, 32 500 mg Suppositories: 120, 125, 30 325, 650 mg
Acetaminophen (Ofirmev)	Infants and children <2 y: limited data available: 7.5–15 mg/kg/dose every 6 h; maximum daily dose: 60 mg/kg/day (Wilson-Smith, 2009) Children ≥2 y and adolescents: <50 kg: 15 mg/kg/dose every 6 h or 12.5 mg/kg/dose every 4 h; maximum single dose: 15 mg/kg up to 750 mg; maximum daily dose: 75 mg/kg/day not to exceed 3,750 mg/day ≥50 kg: 1,000 mg every 6 h or 650 mg every 4 h; maximum single dose: 1,000 mg; maximum daily dose: 4,000 mg/day	Injectable
	NOTE: Contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency. Do not exceed five doses per 24 h. Modify dose in patients with renal impairment	
Acetaminophen and	Dose based on codeine	Elixir:

codeine (Tylenol with codeine)	component: 0.5–1.0 mg/kg/dose Q4–6 h PO	acetaminoph 120 mg and codeine 12 mg/5 mL wi alcohol 7% Suspension, ora alcohol-free acetaminoph 120 mg and codeine 12 mg/5 mL Tabs: Tylenol N 1: acetaminoph 300 mg + codeine 7.5 Tylenol No. 2: acetaminoph 300 mg + codeine 15 r Tylenol No. 3: acetaminoph 300 mg + codeine 30 r Tylenol No. 4: acetaminoph 300 mg + codeine 40 r
Ibuprofen (Motrin, Advil)	4–10 mg/kg/dose Q6–8 h PO	Suspension: 10 mg/5 mL Tabs: 200, 300, 400, 600, 80 mg
	NOTE: Use with caution in patients with aspirin hypersensitivity, hepatic/renal insufficiency or GI disease (bleeding or ulcers).	
Ketorolac	IM, IV: 0.5 mg/kg every 6 h; maximum dose:	

(Toradol)	mg/dose, usual reported duration: 48–72 h; not to exceed 5 days of treatment	
NOTE: Use is contraindicated in patients with advanced renal impairment or patients at risk for renal failure due to volume depletion.		Injectable
Morphine sulfate	Neonates: 0.05–0.2 mg/kg/dose IM/IV Q4h Children: 0.1–0.2 mg/kg/dose IM/IV Q2–4 h	Injectable
	NOTE: May cause respiratory and central nervous system depression. Nalaxone 0.01 mg/kg may be used to reverse effects; repeat every 2–3 min as needed, based on response.	
Local anesthetics		
Bupivacaine (Marcaine)	Maximum dose: 2.5 mg/kg (plain), 3.0 mg/kg (with epinephrine 1:200,000)	0.25% solution 2.5 mg/mL
Lidocaine	Maximum dose: 4.5 mg/kg/dose (plain), 7 mg/kg/dose (with epinephrine 1:200,000)	1% solution = 1 mg/mL
Antibiotics		
Amikacin (Amikin)	Neonates: 75 mg/kg/dose IV/IM Dosing interval: Postnatal age Gestational age: <7 d; >7 d <28 wk: Q24h; Q18h	Injectable

	28–34 wk Q18h Q12h >34 wk Q12h Q8h Children: 15–22.5 mg/kg/24 h ÷ Q8–12 h IV/IM	
	NOTE: Therapeutic levels: 20–30 µg/L (peak); 5–10 µg/L (trough). Infusion rate: infants: 1–2 h; children: 30–60 min. Modify dose in patients with renal impairment	
Amoxicillin (Amoxil)	20–50 mg/kg/24 h ÷ Q8h PO UTI prophylaxis: 25 mg/kg QD	Drops: 50 mg/n (15, 30 mL) Suspension: 12 250 mg/5 m (80, 100, 15 200 mL) Caps: 250, 500 mg Chewab tabs: 125, 25 mg
	NOTE: Modify dose in patients with renal impairment	
Amoxicillin-clavulanic acid (Augmentin)	<40 kg: 20–40 mg/kg/24h ÷ Q8h PO >40 kg: 250–500 mg Q8h PO	Tabs: 250, 500 Chewable ta 125, 250 mg Suspension: 12 250 mg/5 m (75, 150 mL
	NOTE: Incidence of diarrhea is higher than with use o amoxicillin alone. Modify dose in patients with renal impairment	
Ampicillin	Neonates: Postnatal age <7 d: <2,000 g: 50 mg/kg/24 h ÷ Q12h IM/IV >2,000 g: 75 mg/kg/24 h ÷ Q8h IM/IV Postnatal age >7 d: <2,000 g: 75 mg/kg/24 h ÷	Drops: 100 mg/mL (20 mL) Suspension: 12 250 mg/5 m (80, 100, 15 200 mL), 50

	Q8h IM/IV >2,000 g: 100 mg/kg/24 h ÷ Q6h IM/IV Infants and children: 50–100 mg/kg/24 h ÷ Q6h IM/IV/PO	mg/5 mL (1 mL) Caps: 250, 500 mg Injectabl
NOTE:	Modify dose in patients with renal impairment	
Aztreonam (Azactam)	Neonates: Postnatal age <7 d: <2,000 g: 60 mg/kg/24 h ÷ Q12h IM/IV >2,000 g: 90 mg/kg/24 h ÷ Q8h IM/IV Postnatal age >7 d: <2,000 g: 90 mg/kg/24 h ÷ Q8h IM/IV >2,000 g: 120 mg/kg/24 h ÷ Q6h IM/IV Children >1 mo: 90–120 mg/kg/24 h ÷ Q6–8h IM/IV	Injectable
NOTE:	Reduce dose in patients with cystic fibrosis. Modify dose in patients with renal impairment	
Cefazolin (Ancef) (1st generation)	Neonates: Postnatal age <7 d: 40 mg/kg/24 h ÷ Q12h Postnatal age >7 d: <2,000 g 40 mg/kg/d ÷ Q12h >2,000 g 60 mg/kg/d ÷ Q8h Infants (>1 mo) and children: 50–100 mg/kg/24 h ÷ Q8h	Injectable
NOTE:	Modify dose in patients with renal impairment	
Ceftriaxone (Rocephin) (3rd generation)	Infants and children: 50–75 mg/kg/24 h ÷ Q12–24h IM/IV Adults: 1–4 g/24 h ÷ Q12–	Injectable

	24h IM/IV	
Cephalexin (Keflex) (1st generation)	Children: 25–100 mg/kg/24 h ÷ Q6h PO	Caps: 250, 500 mg Drops: 1 mg/mL (10 mL)
	Adults: 250–500 mg Q6h PO	Suspension: 12 mg/5 mL (5 60, 100, 200 mL), 250 mg mL (5, 100, 200 mL)
		Tabs: 250, 500, 1,000 mg
NOTE:	Modify doses in patients with renal impairmen	
Ciprofloxacin (Cipro)	20–30 mg/kg/24 h ÷ Q12h IV/PO	Tabs: 250, 500, 750 mg Injection: 20 mg/20 mL
NOTE:	Not recommended for children <16–18 y. Modify doses in patients with renal impairmen Box warning: Fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including tendinitis and tendon rupture, peripheral neuropathy, and CNS effects. Discontinue ciprofloxacin immediately and avoid the use of fluoroquinolones in patients who experienc any of these serious adverse reactions. Because fluoroquinolones have been associated with serious adverse reactions, reserve ciprofloxacin for use in patients wh have no alternative treatment options for th following indications: acute exacerbation o chronic bronchitis, acute sinusitis, and acut uncomplicated cystitis.	
Gentamicin	Neonates: 2.5 mg/kg/dose	Injectable

	IV/IM Dosing interval: Postnatal age Gestational age <7 d >7 d <28 wk Q24h Q18h 28–34 wk Q18h Q12h >34 wk Q12h Q8h Children: 6–7.5 mg/kg/24 h ÷ Q8h IV/IM Adults: 3–5 mg/kg/d ÷ Q8h IV/IM	
NOTE:	Therapeutic levels: 6–10 µg/L (peak); <2 µg/L (trough). Modify dose in patients with renal impairment	
Metronidazole (Flagyl)	Anaerobic infections: 30 mg/kg/d ÷ Q6h IV/PO *Clostridium difficile* infection: 20 mg/kg/d ÷ Q6h PO	Tabs: 250, 500 Injectable
Nitrofurantoin (Furadantin, Macrodantin)	Children >1 mo: 5–7 mg/kg/24 h ÷ Q6h PO Prophylaxis: 1–2 mg/kg/QD	Suspension: 25 mg/5 mL Ta 50, 100 mg Caps: 25, 50, 1 mg
NOTE:	Contraindicated in infants <1 month of age. Modify dose in patients with renal impairment	
Trimethoprim (TMP)-sulfamethoxazole (Septra)	Dose based on TMP component: 8–10 mg/kg/24 h ÷ Q12h PO Prophylaxis: 2 mg/kg/24 h QD	Suspension: 40 mg TMP pe mL (20, 100 150, 200, 48 mL) Tabs: 80 mg TM (single stren [SS]), 160 m TMP (doubl strength [DS

	NOTE: May cause kernicterus in newborns. Modify dose in patients with renal impairment	
Tobramycin (Tobrex)	Neonates: 2.5 mg/kg/dose IV/IM Dosing interval: Postnatal age Gestational age: <7 d: >7 d <28 wk: Q24h: Q18h 28–34 wk: Q18h: Q12h >34 wk: Q12h: Q8h Children: 6–7.5 mg/kg/24 h ÷ Q8h IV/IM Adults: 3–5 mg/kg/24 h ÷ Q8h IV/IM	Injectable
	NOTE: Therapeutic levels: 6–10 µg/L (peak); <2 µg/L (trough). Modify dose in patients with renal impairment	
Antifungal drugs		
Amphotericin B (Fungizone)	Bladder irrigation: 15–50 mg/d in 1 L sterile water or sorbitol/mannitol irrigation instilled over 24 h Infants and children: Test dose: 0.1 mg/kg/dose IV to a maximum of 1 mg; infuse over 30–60 min. Initial therapeutic dose (if test dose is tolerated): 0.25 mg/kg. The daily dose can then be gradually increased, usually in 0.25 mg/kg increments each subsequent day until the	Injectable

	desired dose is reached. Maintenance dose: 0.25–1 mg/kg/d QD, infuse over 2–6 h.	
	NOTE: Modify dose in patients with renal impairment	
Fluconazole (Diflucan)	Children (3–13 y): Loading dose: 10 mg/kg IV/PO Maintenance (begin 24 h after loading dose): 3–6 mg/kg/24 h IV/PO QD	Tabs: 50, 100, 2 mg Injectabl
	NOTE: PO and IV doses are equivalent. Modify dose in patients with renal impairment	
Flucytosine (5-FC)	Neonates: 20–40 mg/kg/dose Q6h PO Children and adults: 50–150 mg/kg/d ÷ Q6h PO	Caps: 250, 500 mg
	NOTE: Modify dose in patients with renal impairment	
Antiemetics		
Ondansetron (Zofran)	Children >3 y: 0.15 mg/kg/dose IV Q4h	Injectable
	NOTE: Decreased effectiveness has been reported wh administered for more than 3 doses.	
Prochlorperazine (Compazine)	Oral, rectal: 0.4 mg/kg/24 h ÷ Q6–8h PO/PR IM: 0.1–0.15 mg/kg/dose TID	Injectable Tabs: 5, 10, 25 Syrup: 5 mg/5 r (120 mL) Suppository: 2. 5, 25 mg
	NOTE: Safety and efficacy have not been established children <9 kg or <2 y of age.	
Trimethobenzamide (Tigan)	Children: Oral, rectal: 15–20 mg/kg/d ÷ 3–4 doses IM: Not recommended Adults: Oral: 250 mg 3–4 times/24	Injectable Caps: 100, 250 mg Suppository 100, 200 mg

	h IM, rectal: 200 mg 3–4 times/24 h	
	NOTE: Contraindicated in neonates and premature infants.	
Anti-enuresis drugs		
Desmopressin acetate (DDAVP)	Nocturnal enuresis (>6 y): 20 µg at bedtime intranasally Range 10–40 µg	Spray: 5-mL bottle with spray pump delivering 5 doses of 10
Imipramine (Tofranil)	Nocturnal enuresis (>6 y): Initial: 10–25 mg QHS PO Increment: 10–25 mg/dose at 1–2 wk intervals until maximal dose for age or desired effect achieved	Tabs: 10, 25, 5(mg Caps: 75, 100, 125, 150 mg
	NOTE: Maximal dose: 6–12 y: 50 mg/24 h; 12–14 y: mg/24 h or 2 mg/kg/d. Boxed warning: Antidepressants increased the risk compared with placebo of suicidal thinking and behavior (suicidality) in short term studies in children, adolescents, and young adults with major depressive disorde (MDD) and other psychiatric disorders. Anyone considering the use of imipramine any other antidepressant in a child, adolescent, or young adult must balance th risk with the clinical need. Short-term studi did not show an increase in the risk of suicidality with antidepressants compared with placebo in adults older than 24 years; there was a reduction in risk with antidepressants compared with placebo in adults 65 years and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are	

	started on antidepressant therapy should be monitored appropriately and observed clos for clinical worsening, suicidality, or unusu changes in behavior. Families and caregive should be advised of the need for close observation and communication with the health care provider. Imipramine is not approved for use in pediatric patients excep for patients with nocturnal enuresis.	
Bladder analgesics		
Phenazopyridine (Pyridium)	Children 6–12 y: 12 mg/kg/24 h ÷ TID	Tabs: 100, 200
	NOTE: Colors urine orange, may also stain contact lenses and clothing.	
Histamine$_2$ blockers		
Cimetidine (Tagamet)	Neonates: 5–10 mg/kg/d ÷ Q8–12h PO/IV/IM	Tabs: 200, 300, 400, 800 mg
	Infants: 10–20 mg/kg/d ÷ Q6–12h PO/IV/IM	Syrup: 300 mg/ mL (237 mL
	Children: 20–30 mg/kg/d ÷ Q6h PO/IV/IM Adults: 300 mg/dose Q6h PO/IV/IM, 400 mg/dose Q12h, or 800 mg/dose QHS	Injectable
	NOTE: Modify dose in patients with renal impairment	
Ranitidine (Zantac)	PO: 2–4 mg/kg/24 h ÷ Q12h	Tabs: 150, 300
	IV: 1–2 mg/kg/24 h ÷ Q8–8h	Syrup: 15 mg/m (7.5% alcoh
	NOTE: Modify dose in patients with renal impairment	
Drug therapy for neurogenic bladder dysfunction		
Anticholinergic		
Hyoscyamine (Levsin)	SL tabs: Children 2–12 y: 1/2 to 1 tab Q4h. Do not exceed 6 tabs in 24 h 12 y of age and older: 1–2	SL tabs: 0.125

	tabs Q4h. Do not exceed 12 tabs in 24 h or 0.03 mg/kg BID–0.1 mg/kg QID	
Oxybutynin (Ditropan)	Children <5 y: age in y = mL per dose BID/TID >5 y: 0.2 mg/kg BID-QID	Tabs: 5 mg Syrup: 5 mg/5 r (473 mL)
Propantheline (Pro-Banthine)	0.5 mg/kg BID-QID	Tab: 7.5, 15 mg
Sympathomimetic		
Pseudoephedrine (Sudafed)	0.4 mg/kg BID–0.9 mg/kg TID	Tabs: 30, 60 mg Liquid: 15 mg/5 mL (120 mL 30 mg/5 mL (120 mL, 24 mL, 473 mL
Sympatholytic		
Tamsulosin (Flomax)	Children >3 y: Initial dose 0.2 mg once daily, increase by 0.2 mg increments based on response (symptoms and urodynamic studies) and tolerability. Maximum reported daily dos 0.8mg/day	
		Caps: 0.4 mg
Hormonal treatment of retractile testes		
Chorionic gonadotropin (Pregnyl)	50 USP U/kg IM Q5d × 5 doses	Injectable
	NOTE: Maximal single dose 2,000 USP U. Maximal total dose 10,000 USP U.	
Cathartics		
Bisacodyl (Dulcolax)	Oral: Children 3–12 y: 5–10 mg or 0.3 mg/kg/d as a single dose Suppository: Children <2 y: 5 mg/d as a single dose Children 2–	Tabs: 5 mg Suppository: 5, mg

	11 y: 5–10 mg/d as a single dose	
Docusate (Colace)	<3 y: 10–40 mg/24 h ÷ QD-QID 3–6 y: 20–60 mg/24 h ÷ QD-QID 6-12 y: 40–120 mg/24 h ÷ QD-QID >12 y: 50–500 mg/24 h ÷ QD-QID	Caps: 50, 100, 240, 250, 30 mg Tabs: 50, 100 m Syrup: 20 mg/5 mL (240 mL
Mineral oil	5–11 y: 5–20 mL QD >12 y: 15–45 mL QD	Emulsion: 1.4 g mL (480 mL
Polyethylene glycol (Miralax)	0.2–0.8 g/kg/d, maximum dose 17 g/d	2.5 mL/5 mL (420 mL), 2 mL/5 mL (4 mL), 4.75 mL/5 mL (2 mL) Liquid: 500, 10 4000 mL
Senna (Senokot)	Oral: Children: 10–20 mg/kg/dose at bedtime Rectal: Children >27 kg: 1/2 suppository at bedtime	Granules: 325 mg/teaspoon Liquid: 7% (13 mL, 360 mL 6.5% (75 mg 150 mL) Syrup: 218 mg/ mL (60 mL, 240 mL) Tab: 187, 217, 600 mg Suppository rectal: 652 m

NOTE: Maximal dose = 872 mg.

From Stock JA, Packer MG, Kaplan GW. Pediatric urology facts and figures: data useful in the management of pediatric urologic patients. *Urol Clin N Am* 1995;22:205–219.

III. DRUG DOSAGES IN RENAL INSUFFICIENCY

A. Drug dosage in patients with renal insufficiency (Table 33-2) may be adjusted by the following.

1. Interval extension (IE): Lengthen the interval between doses, keeping the dosage size normal, or
2. Dose reduction (DR): Reduce the amount of individual doses, keeping the interval between doses normal.

TABLE 33-2 Drug Dosages in Renal Insufficiency

Drug	Normal Dose Interval	Method	Creatini (mL/mi >50
Antibiotics			
Amikacin	Q8–12 h	IE	Q12 h Q12–18h
		DR	60–90% 30–70%
Amoxicillin	Q8 h	IE	Q8 h Q8–12 h
Amoxicillin and clavulanic acid	Q8 h	IE	Q8 h Q12–18 h
Ampicillin	Q4–6 h	IE	Q6 h Q6–12 h
Aztreonam	Q6–8 h	DR	100% 50%
Cefazolin	Q8 h	IE	Q8 h Q8–12 h
Cefixime	Q12–24 h	DR	100% 75%
Cephalexin	Q6 h	IE	Q6 h Q6–8 h
Ciprofloxacin	Q12 h	IE	Q12 h Q18–24 h
Gentamicin	Q8 h	IE	Q8–12 h Q12 h
		DR	60–90% 30–70%

Nitrofurantoin	Q8 h	IE	Q8 h	Avoid
Sulfamethoxazole	Q12 h	IE	Q12 h	Q18 h
Trimethoprim	Q12 h	IE	Q12 h	Q18 h
Tobramycin	Q8h	IE	Q8–12 h	Q12h
		DR	60–90%	30–70%
Antifungal				
	Amphotericin B	Q24 h	IE	Q24 h
	Fluconazole	QD	DR	100%
	Flucytosine	Q6 h	IE	Q6 h
			DR	50%
Nonantibiotics				
	Acetaminophen	Q4 h	IE	Q4 h
	Cimetidine	Q12 h	IE	Q6 h
			DR	100%
	Ranitidine	Q8–12 h	DR	100%

From Stock JA, Packer MG, Kaplan GW. Pediatric urology facts and figures: data useful in the management of pediatric urologic patients. *Urol Clin N Am* 1995;22:205–219.

B. Note: These drug-dosage modifications are approximations. Patients must be followed closely for signs of toxicity.

IV. BOWEL PREPARATION

See Table 33-3.

TABLE 33-3 Bowel Preparation

Drug	Dose	Supplied As
Magnesium citrate	4 mL/kg/dose PO. Repeat Q4–6 h until	Solution 300 mL

	liquid stool results Note: Maximal dose = 200 mL. Use with caution in patients with renal insufficiency.	
Polyethylene glycol electrolyte solution (GoLYTELY)	Oral: 25–40 mL/kg/h until rectal effluent is clear Nasogastric: 20–30 mL/min to 4 L (1.2–1.8 L/h) Note: Monitor electrolyte levels with prolonged administration. Rapid drinking of each portion is preferred to drinking of small amounts continuously.	Powder for oral solution: 2,000 mL, 4,000 mL, 4,800 mL, 6,000 mL
Neomycin	Preoperative intestinal antisepsis: Children: 25 mg/kg PO at 1, 2, and 11 p.m. on day preceding surgery Adults: 1 g PO at 1, 2, and 11 p.m. on day preceding surgery	Tab: 500 mg Solution: 125 mg/5 mL (480 mL)
Erythromycin	Preoperative intestinal antisepsis: Children: 20 mg/kg base PO at 1, 2, and 11 p.m. on day preceding surgery Adults: 1 g base PO at 1, 2, and 11 p.m. on day preceding surgery	Caps: 125, 250 mg

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V. FORMULAS

A. **Ideal Body Weight** (children 1 to 18 years) in kg = [height^2 (cm) × 1.65]/1000

B. **Body Surface Area** (Fig. 33-1)

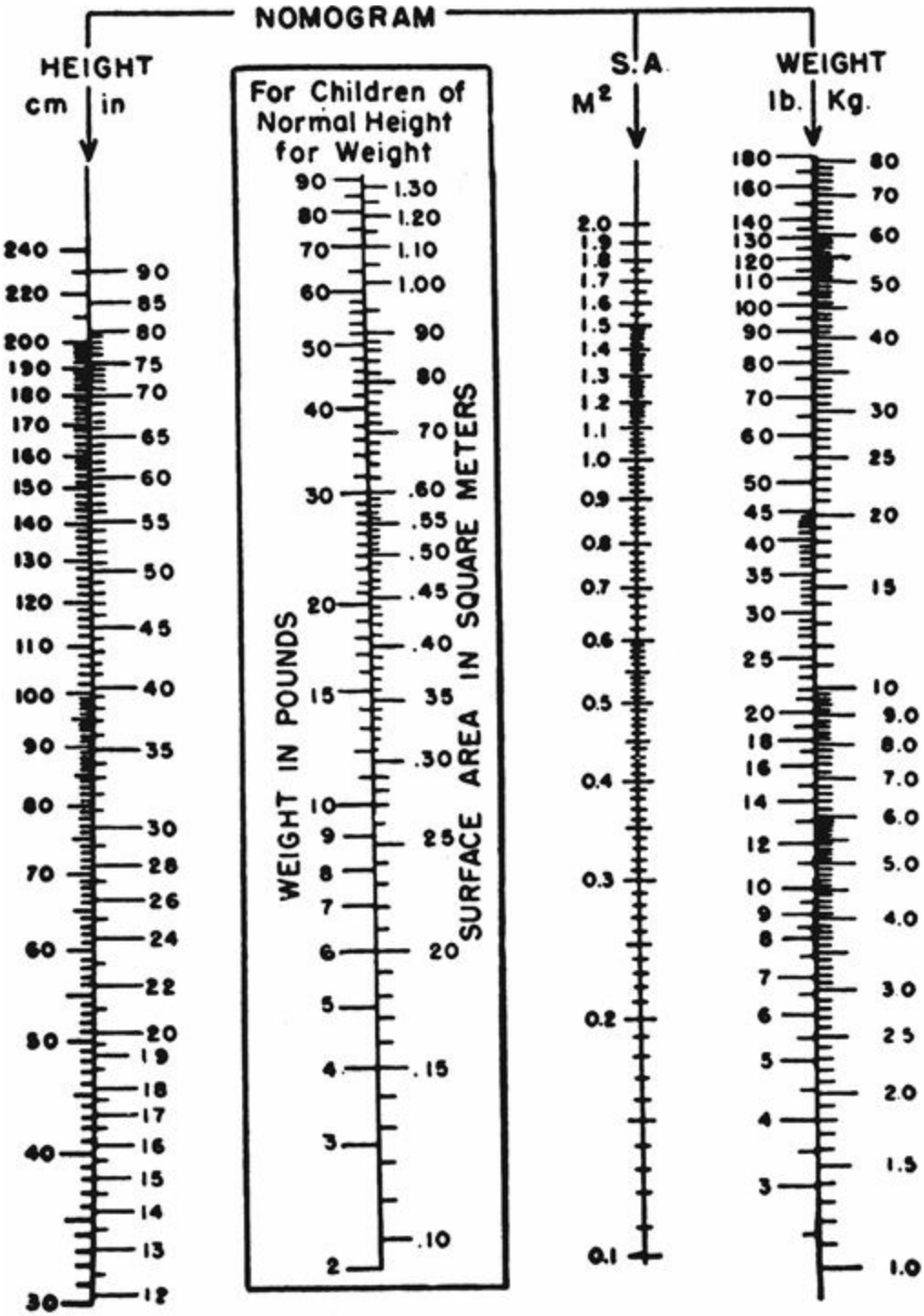

Fig. 33-1 Nomogram or estimation of surface area. The surface area is indicated when a straight line that connects the height and weight levels intersects the surface area column; or the patient is roughly of average size, from the weight along (enclosed area). (From Behrman RE, Kliegman RM. *Nelson Textbook of Pediatrics*, 13th ed. Philadelphia, PA: WB Saunders; 1987:1521.)

C. Creatinine Clearance

1. Estimation of creatinine clearance using body length
   Creatinine clearance (mL/min/1.73 m^2) = [K × length (cm)]/serum creatinine (mg/dL)
   where K = constant that is age specific
   a. Low birth weight, 1 year or younger: $K = 0.33$
   b. Full-term, 1 year or younger: $K = 0.45$
   c. Boys and girls, 7 to 12 years old: $K = 0.55$
   d. Girls, 13 to 21 years old: $K = 0.55$
   e. Boys, 13 to 21 years old: $K = 0.70$
2. Estimation of creatinine clearance using body surface area (BSA) Children 1 to 18 years old:
   Creatinine clearance (mL/min/1.73 m^2) = 0.48 × height (cm) × BSA
   serum creatinine level (mg/dL) × 1.73
3. Nomogram (Fig. 33-2)

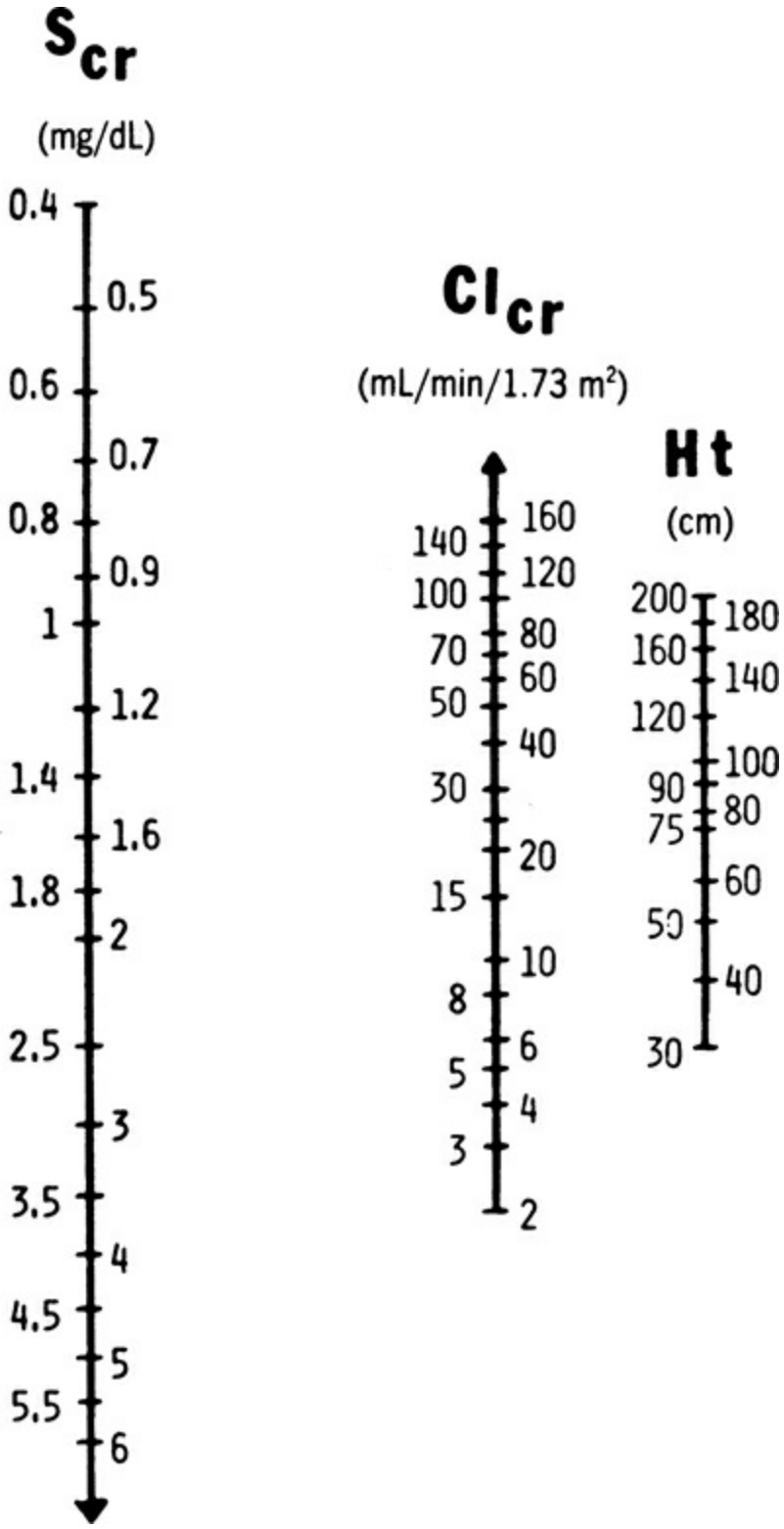

Fig. 33-2 Nomogram for rapid evaluation of endogenous creatinine clearance in children (1 to 18 years of age). To predict creatinine clearance, connect the child's serum creatinine concentration and height with a ruler and read the creatinine clearance where the ruler intersects the central line.

(From Traub SL, John CE. Comparison of methods of estimating creatinine clearance in children. *Am J Hosp Pharm* 1980;37:195.)

4. Normal values for glomerular filtration rate in children (Fig. 33-3)

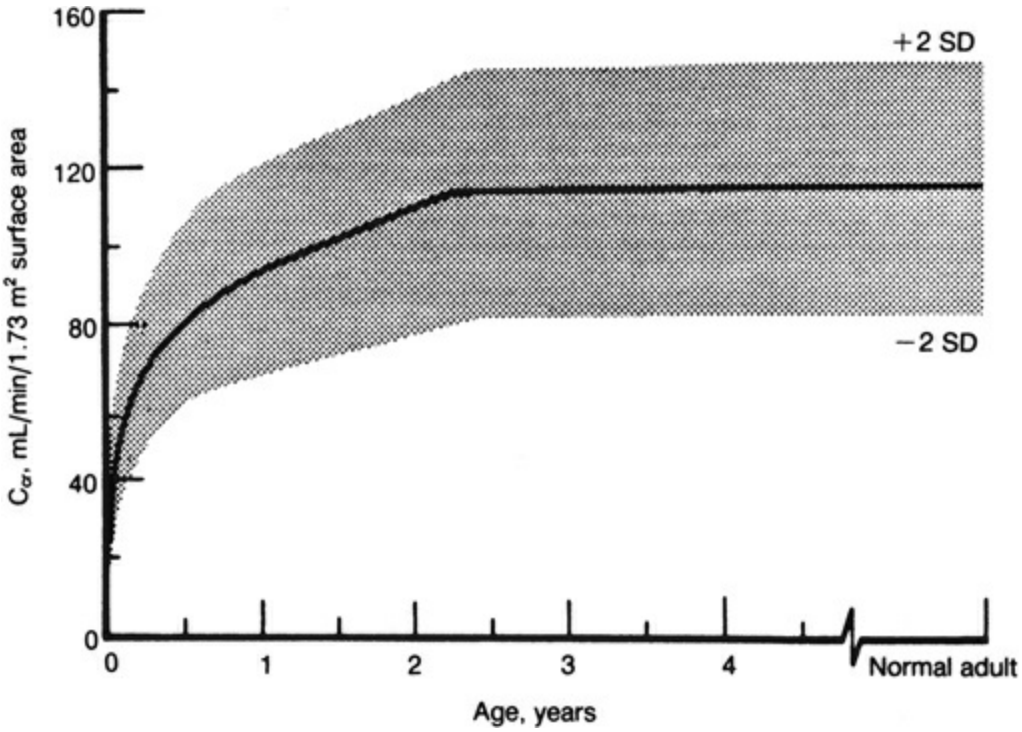

Fig. 33-3 Changes in normal value for glomerular filtration rate (GFR) from birth to later childhood. The GFR was derived by endogenous creatinine clearance. (From McCrory WN. *Developmental Nephrology*. Cambridge, MA: Harvard University Press; 1972:98. Graph created from data from Winberg J. The 24 hour true endogenous creatinine clearance in infants and children without renal disease. *Acta Pediatr* 1959;48:443–452.)

D. **Bladder Capacity**
   1. Children younger than 2 years: bladder capacity (mL) = 7.0 × weight (kg)
   2. Children 2 to 11 years old: bladder capacity (mL) = [age (years) + 2 × 30]

E. **Normal Stretched Penile Length** (Fig. 33-4)

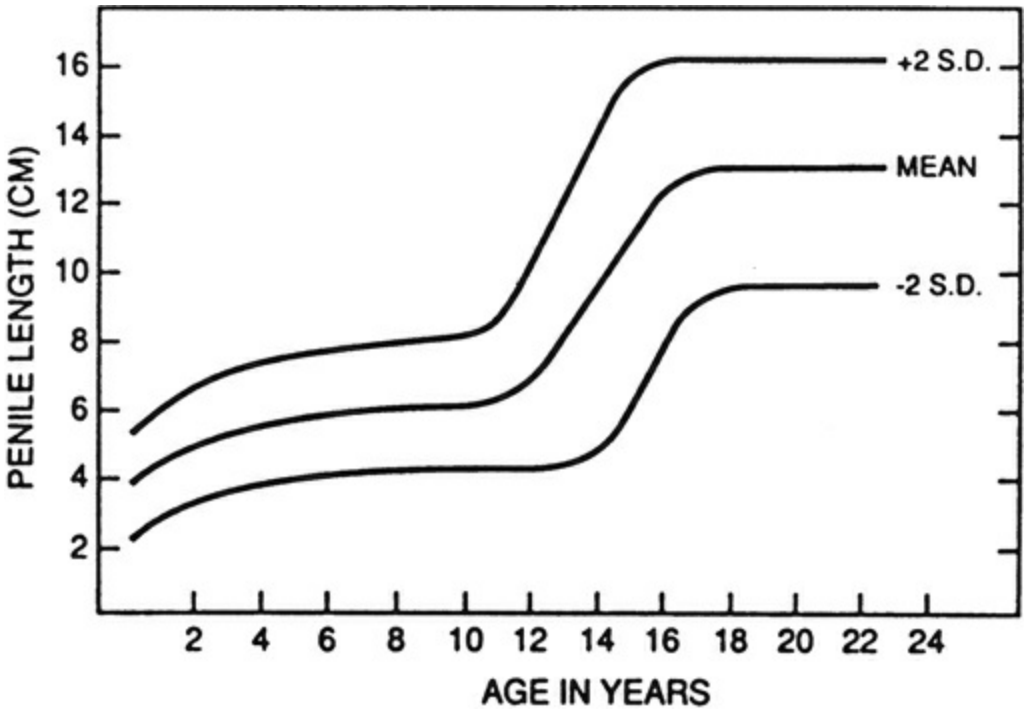

Fig. 33-4 Nomogram of the normal range of stretched penile length in men as a function of age (SD). (From Griffin JE, Wilson JD. Disorders of sexual differentiation. In: Walsh PC, Retik AB, Stamey TA, et al., eds. *Campbell's Urology*, 6th ed. Philadelphia, PA: WB Saunders; 1992:1531.)

F. **Vital Signs** (Table 33-4)

TABLE 33-4 Normal Values for Vital Signs in Children up to 10 Years of Age

Age (y)	Pulse Rate (beats/min)	Blood Pressure (mm Hg)	Respirations (breaths/min)
0–1	120	80/40	40
0–5	100	100/60	30
5–10	80	120/80	20

From Coran AG. Perioperative care of the pediatric surgical patient. *Sci Amer Surg* 1994;VIII:3, with permission.

G. **Blood Pressure** (Table 33-5)

TABLE 33-5 Classification of Hypertension by Age Group

Age Group	Significant Hypertension (mm Hg)	Severe Hypertension (mm Hg)
Newborn (7 d)		
Systolic BP	≥96	>106
Newborn (8–30 d)		
Systolic BP	≥104	≥110
Infant (<2 y)		
Systolic BP	≥112	≥118
Diastolic BP	≥74	≥82
Children (3–5 y)		
Systolic BP	≥116	≥124
Diastolic BP	≥76	≥84
Children (6–9 y)		
Systolic BP	≥122	≥130
Diastolic BP	≥78	≥86
Children (10–12 y)		
Systolic BP	≥126	≥134
Diastolic BP	≥82	>90
Adolescents (13–15 y)		
Systolic BP	≥136	≥144
Diastolic BP	≥86	≥92
Adolescents (16–18 y)		
Systolic BP	≥142	≥150
Diastolic BP	≥92	≥98

BP, blood pressure. From Task force on blood pressure control in children: report on the second task force on blood pressure control in children. *Pediatrics* 1987;7:1, with permission.

H. **Renal Length versus Age** (Fig. 33-5A), **Height** (Fig. 33-5B), **Weight** (Fig. 33-5C), **and Total BSA** (Fig. 33-5D)

Age based formula for predicting renal length in children

In children 1 year of age or older: Length (cm) = age (years) × 0.3 + 6

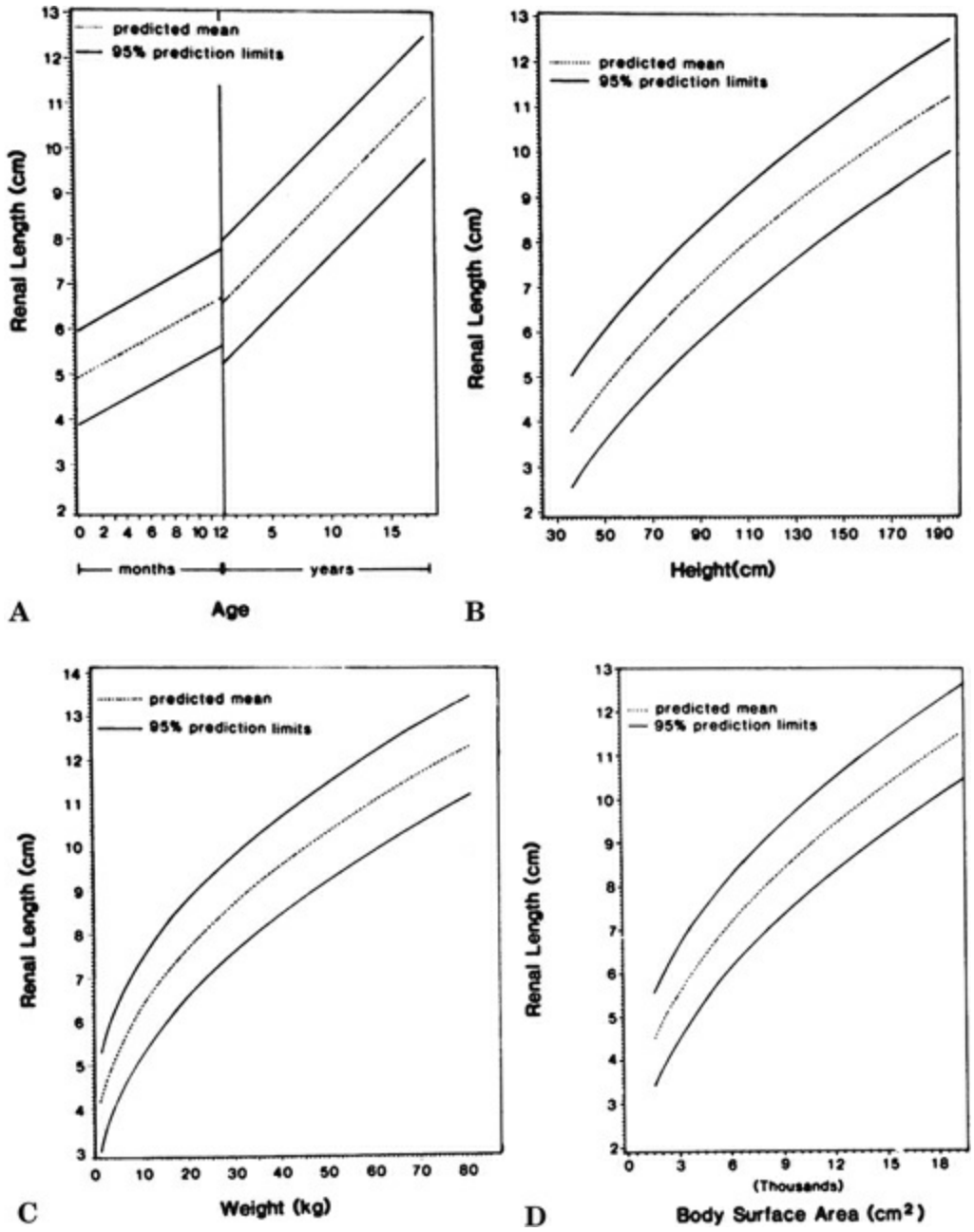

Fig. 33-5 Renal length versus (A) age, (B) height, (C) weight, and (D) total body surface area. Dashed line, predicted mean; solid line, 95% prediction limits. (From Han BK, Babcock DS. Sonographic measurements and appearance of normal kidneys in children. *Am J Roentgenol* 1985;145:611.)

I. **Physical Development** (Table 33-6)

TABLE 33-6 Physical Development

Term neonates may lose up to 10% of their birth weight in the first few days of life and typically regain their birth weight by 10 to 14 days.
Newborns gain approximately 30 g per day (1 oz per day) until 3 months.
Infants gain approximately 20 g per day (0.67 oz per day) between 3 and 6 months of age and approximately 10 g per day between 6 and 12 months.
Infants double their birth weight by 4 months and triple their birth rate by 1 year.
Children gain 2 kg per year (4.4 lbs per year) between 2 years and puberty.
The average length at birth for a term infant is 20 in. (50 cm).
Infants grow 4 in. (25 cm) during the first year of life.
Toddlers grow 4 in. (10 cm) between 12 and 24 months, 3 in. (7.5 cm) between 24 and 36 months, and 3 in. (7.5 cm) between 36 and 48 months.
Children reach half their adult height by 24 to 30 months.
Children grow 2 in. per year (5 cm per year) between age 4 years and puberty.
There is normal deceleration of height velocity before the pubertal growth spurt.

From Nichols J. Normal growth patterns in infants and prepubertal children. Duryea, T. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com (accessed November 5, 2017).

J. **Tanner Stages** (Fig. 33-6)

	Breast	Pubic Hair	Genitals	Pubic Hair
Stage 1	Small nipples. No breast.	No pubic hair.	No signs of puberty. Scrotum, testes, and penis as in childhood.	No pubic hair.
Stage 2	Breast and nipples have just started to grow. The areola has become larger. Breast tissue bud feels firm behind the nipple.	Initial growth of long pubic hairs. These are straight, without curls, and of light color.	Initial growth of scrotum and testes. The skin on the scrotum has become redder, thinner, and more wrinkled. The penis may have grown a little in length.	Few hairs around the root of the penis. The hairs are straight, without curls, an of light color.
Stage 3	Breast and nipples have grown additionally. The areola has become darker. The breast tissue bud is larger.	The pubic hair is more widespread. The hair is darker, and curls may have appeared.	The penis has now grown in length. Scrotum and testes have grown. The skin of the scrotum has become darker and more wrinkled.	Hairs are darker and curlier and still sparse, mostly located at the penis root.
Stage 4	Nipples and areolas are elevated and form an edge towards the breast. The breast has also grown a little larger.	More dense hair growth with curls and dark hair. Still not entirely as an adult woman.	The penis has grown in both length and width. The head of the penis has become larger. The scrotum and testes have grown.	More dense, curly, and dark hair. The hair growth is reaching the inner thighs.
Stage 5	Fully developed breast. Nipples are protruding, and the edge between areola and breast has disappeared.	Adult hair growth. Dense, curly hair extending towards the inner thighs.	Penis and scrotum as an adult.	Pubic hair extends upwards to the umbilicus. It is dense and curly.

Fig. 33-6 Tanner stages.From Morris NM, Udry JR. Validation of a self-administered instrument to assess stage of adolescent development. *J Youth Adolesc* 1980;9(3):271–280.

TABLE 33-7 Urine Output per Day According to Age

Age	Output (cc)
0–48 h	15–60

3–10 d	100–300
10–60 d	250–450
2 mo–1 y	400–500
1–3 y	500–600
3–5 y	600–700
5–8 y	650–1,000
8–14 y	800–1,400

From Campbell M. *Clinical Pediatric Urology*. Philadelphia,PA: WB Saunders; 1951.

K. **Urine Output and Voiding Habits** (Tables 33-7 and 33-8)

TABLE 33-8 Percentile Information for Elimination by Age Group

Age Group (y)	Number of Patients	Voids per Day		Bowel Movements per Week	
		10th	90th	10th	90th
2 or less	34	4.3	9.0	5.0	10.6
3	137	3.5	7.5	5.0	12.0
4	149	3.5	7.0	5.0	10.0
5	118	3.5	7.0	4.0	9.0
6	100	3.2	7.5	4.0	7.3
7	101	3.0	7.0	4.2	8.8
8	79	3.0	7.0	4.2	7.9
9	78	3.0	7.0	4.0	7.9
10	76	3.5	7.0	4.0	8.8
11	64	3.5	7.0	4.0	8.9
12	56	3.0	7.6	4.0	10.2
13	45	3.0	5.5	3.5	9.0
14	33	3.4	9.0	3.0	10.0
15	33	3.0	7.0	3.6	8.7
16	25	3.0	7.2	1.9	14.0
17	23	3.0	5.5	3.6	9.0
18 or more	41	3.0	8.2	4.0	8.1

From Bloom DA, Seeley WW, Ritchey ML, et al. Toilet habits and continence in

children: an opportunity sampling in search of normal parameters. *J Urol* 1993;149:1087, with permission.

RECOMMENDED READING

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Stock JA, Packer MG, Kaplan GW. Pediatric urology facts and figures: data useful in the management of pediatric urologic patients. *Urol Clin North Am* 1995;22:205–219.

Taketomo CK, Hodding JH, Kraus DM. *Pediatric and Neonatal Dosage Handbook,* 23rd ed. Cleveland, OH: Lexi-Comp; 2016.

34 Online Pediatric Urology Recommendations

Laurence S. Baskin and Jeffrey A. Stock

The Internet is ubiquitous and patients and physicians have easy access to an unlimited amount of unreferenced medical material. The trick is to negotiate the web in a strategic fashion so that reliable, accurate, and up-to-date information can be obtained. Below are monitored websites that give useful patient information on common pediatric urology problems, including patient handouts in both English and Spanish.

One of the most important pieces of information that can be obtained on the Internet is a physician in your community with expertise in pediatric urology. Urologists who have obtained further training in pediatric urology and confine their practice to children can be found by searching the membership list of the Society of Pediatric Urology at http://www. spuonline.org/

RECOMMENDED PEDIATRIC UROLOGY WEBSITES

Pediatric Urology

American Urological Association (AUA) Guidelines

Cryptorchidism: www.auanet.org/guidelines/vesicoureteral-reflux

Vesicoureteral reflux: http://www.auanet.org/guidelines/cryptorchidism

American Academy of Pediatrics (AAP) Guidelines

Urinary tract infection: Clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months old: http://pediatrics.aappublications.org/content/128/3/595

Circumcision: http://pediatrics.aappublications.org/content/130/3/585

Timing of elective surgery on the genitalia of male children with particular reference to the risks, benefits, and psychological effects of surgery and anesthesia: http://pediatrics.aappublications.org/content/97/4/590

http://urology.ucsf.edu/clinicalRes/CRpedUro.html

www.urologyhealth.org

www.mayoclinic.org

Hypospadias

hypospadias.com

http://urology.ucsf.edu/clinicalRes/CRhypo.html

General Urology Health Information

http://urologyhealth.org.

Learning the Society for Fetal Urology (SFU) Method to Grade Hydronephrosis

http://cevlforhealthcare.org/cevl/Products/Urology/SFU-GradingSystem/mobile/index.html

Pediatric Urology Patient Handouts

http://urology.ucsf.edu/patientGuides/pedUro.html

English Version

- Bladder augmentation surgery
- Children's continence clinic
- Circumcision: postoperative instructions for newborn, baby, and toddler

- Circumcision: postoperative instructions for adolescents
- Clean intermittent catheterization for bladder emptying
- Clean intermittent catheterization through an abdominal stoma (appendicovesicostomy)
- Enuresis (bedwetting)
- Hydrocele/hernia
- Hydronephrosis: prenatal diagnosis
- Hypospadias overview
- Hypospadias repair and postoperative care
- Length of stay for specialized pediatric urologic care
- Pediatric urinary continence
- Pyeloplasty surgery for ureteropelvic junction (UPJ) obstruction
- Undescended testes
- Ureteral reimplant surgery for reflux
- Urinary tract infection (UTI)
- Voiding cystourethrogram (VCUG)
- Vesicoureteral reflux

Spanish Version

- Clínica de continencia de niños en Español
- Enuresis en Español
- Hernia/hidrocele en Español
- Hipospadias en Español
- Undescended testes en Español: el testiculo retenido (no ha decendido)
- Ureteral reimplant surgery en Español: cirugia de reimplantacion ureteral
- VCUG en Español: cistouretrograma de evacuacion de orina

INDEX

Page numbers with "*f*" and "*t*" denote figures and tables, respectively.

A

ABH antigen system testing, in transplantation, 214–215
Abnormalities of sexual differentiation, 29–43
  46,XX gonadal and ductal development, 31
  46,XY DSD, 36, 42t
  46,XY gonadal and ductal development, 30–31
  46,XY pure gonadal dysgenesis (Swyer syndrome), 39t
  absent testes syndrome in, 24–25, 39t
  androgen synthesis, 41f
  chromosomal sex disorders in, 29
  complete androgen insensitivity, 39t, 49
  congenital adrenal hyperplasia in, 35
  desmolase deficiency, 40t
  disorders of sex development (DSDS), 31–32
  embryonic development, 29
  endocrine function, 30–31
  genetic testing, 34
  history, 32–35
  3β-hydroxysteroid dehydrogenase deficiency, 40t
  17β-hydroxysteroid dehydrogenase deficiency, 40t
  17α-hydroxylase deficiency, 40t
  21α-hydroxylase deficiency, 33, 35–41
  imaging and other objective data, 34
  laboratory evaluation, 33–34
  Leydig cell differentiation, 30
  Leydig cell hypoplasia, 39t
  mixed gonadal dysgenesis (MGD) in, 34, 36, 38t

newborns, diagnosis and treatment of common disorders in, 35–43
normal sexual differentiation, 29
ovarian development, 31
overtesticular DSD, 41
partial androgen insensitivity, 39t
penile length chart for, 33t, 307, 309f
persistent müllerian duct syndrome, 39t
physical examination, 33
primordial germ cells (PGCs) and, 29, 31
5α-reductase deficiency, 40t
sex determining factor (SRY) and, 29, 31
sex of rearing, 34–35
steroidogenic acute regulatory protein deficiency, 40t
surgery, 34
testicular feminization in, 49
testosterone production, 31
typical sex differentiation, 29
Absent testes syndrome, 24–25, 39t
Acetaminophen and codeine, 296t
Acetaminophen (Tylenol), 17, 248, 296t, 305t
Acidosis, 204, 210
Acute interstitial nephritis, 201
Acute kidney injury (AKI), 201–205, 202t, 203t, 305, 305t
Acute scrotum, 159–162. *See also* Testicular torsion
bacterial epididymitis, 161–162
testicular torsion in, 159–161
torsion of appendix testis/epididymis, 159
Acute tubular necrosis (ATN), 201
Adhesions, labial, 269, 270f
Adolescent urology, 159–166. *See also* Gynecology, pediatric/adolescent
benign childhood urethrorrhagia, 162–163
delayed puberty in, 164–166. *See also* Abnormalities of sexual differentiation
epididymitis in, 160t, 161–162
gynecology, pediatric. *See* Gynecology, pediatric/adolescent
testicular or epididymal appendix torsion (acute scrotum) in, 159, 160t, 161f

varioceles in, 163–164, 163f
Alemtuzumab, as T cell antibody therapy in transplantation, 218
Alpha adrenergics, in spina bifida and sphincter function, 101
Alpha blockers, urinary incontinence (daytime) and, 79
Alpha fetoprotein (AFP), 96, 232, 273
Alport syndrome, 183, 184, 207
Alveolar tumors, 226
Amenorrhea. *See* Gynecology, pediatric/adolescent
Amikacin (Amikin), 297t, 305t
Amlodipine, 205, 210
Amoxicillin (Amoxil), 64t, 108, 298t, 305t
Amoxicillin-clavulanic acid (Augmentin), 298t, 305t
Amphotericin B (Fungizone), 301t, 305t
Ampicillin, 298t, 305t
Anal examination, 262, 263f
Analgesics, 296–297t, 302t
Anderson-Hynes dismembered pyeloplasty procedure, in hydronephrosis, 116
Androgen synthesis, 41f
Anemia, 204, 210
Anesthesia, 6, 11, 241–247, 242f, 297t. *See also* Pain control in children
Angiographic embolization, 172
Angiomyolipoma (AML), 231, 250
Angiotensin converting enzyme (ACE) inhibitors, chronic kidney disease (CKD) and, 209–210
Anti-reflux flap-valve mechanism, 145
Antibiotics/antifungals/antivirals. *See specific medications*
Anticholinergics, 63, 79, 84, 98, 99, 137, 303t
Antidepressants, urinary incontinence (daytime) and, 79
Antidiuretic hormone (ADH), 82, 137
Antiemetics, pediatric dosage of, 301–302t
Antienuresis drugs, pediatric dosage of, 302t
Antigen system testing in transplantation, ABH and HLA systems in, 214–215
Antilymphocyte globulin, 219
Antimetabolites, immunosuppression in transplantation using, 218
Antithymocyte globulin (Atgam), as T cell antibody therapy in

transplantation, 218
Appendix, in testicle or epididymis, 159, 161f
APSGN type glomerulonephritis, 184–185
Aromatase, 31
Artificial urinary sphincter, 102, 103f
Ascending testes, 21
Asymptomatic bacteriuria, 55
Atgam. *See* Antithymocyte globulin
Augmentin. *See* Amoxicillin-clavulanic acid
Autosomal recessive polycystic kidney disease (ARPKD), 215
Azathioprine, immunosuppression in transplantation using, 218
Azotemia, 201, 204
Aztreonam (Azactam), 298t, 305t

B

Bacterial epididymitis, 161–162
Bacteriuria, 55, 72, 102
Basiliximab, immunosuppression in transplantation using, 218
Beckwith-Wiedemann syndrome, Wilms tumor and, 227, 244
Bed wetting. *See* Nocturnal enuresis
Bedwetting alarm, for nocturnal enuresis, 84f, 85
Behavior modification therapy for incontinence/enuresis, 78
Belatacept, 219
Benign childhood urethrorrhagia, 162–163
Benign familial hematuria in, 183
Benign urinary frequency, urinary incontinence (daytime) and, 71, 74, 80
Beta-human chorionic gonadotropin (β-hCG), 273
Betamethasone ointment, in phimosis and paraphimosis, 2
Biofeedback training, 80, 92
Biopsy, in chronic kidney disease (CKD), 209
Bipotential cells, differentiation of, 31
Bisacodyl (Dulcolax), 304t
Bladder
abnormalities of, and UTIs, 52
artificial urinary sphincter for, 102, 103f
benign urinary frequency, 71, 74, 80
bladder neck suspension and reconstruction in, 102

bowel bladder dysfunction and, 70, 80
capacity of, calculating, 306–307, 310
control of, development of, 69
cystoscopy in, 78
exstrophy and, 60
fractionated or incomplete voiding in, 76
giggle incontinence and, 71–72, 74
lazy bladder, 71, 74, 80
nephrogenic adenoma in, 233–234
neurogenic, and UTIs, 53
nocturnal enuresis (bed wetting) and, 72, 81–85. *See also* Nocturnal enuresis
nonneurogenic neurogenic bladder (NNNB; Hinman syndrome), 70, 80
obstruction of, 60
pelvic floor dysfunction (PFD) in, 70
prune belly (Eagle-Barrett) syndrome and, 154
renal and bladder ultrasound (RBUS), 60, 62
rhabdomyosarcoma and, 226, 227
spina bifida and, 95–106
staccato (intermittent stream) voiding and, 75–76
surgical augmentation of, 99–101, 100f, 138, 151
transient wetting and, 71, 80
transitional cell carcinoma in, 234
traumatic injury to, 173–174
tumors of, 233–234
ultrasound/sonogram examination of, 76, 83
uninhibited (unstable, overactive or spastic), 71, 74, 80, 87
urachal anomalies in, 141, 143
urethral valves in, 108
vesicoureteral reflux and, 72, 87
vesicovaginal voiding and, 71, 74, 80
video urodynamic study in, 77–78
voiding cystourethrogram (VCUG) in, 56, 59, 62, 77, 114, 116, 121, 124, 127, 130, 135
voiding diary for, 74–75, 75–76f
voiding dysfunction and, 70, 70f, 72, 73f, 74
voiding frequency disorders and, 80

x-ray imaging of, 77
Bladder and bowel dysfunction (BBD), 60–61
Bladder exstrophy (BE), 143, 145, 285–286
Bladder neck reconstruction (BNR), 147
Bladder neck suspension and reconstruction, in spina bifida and urologic function, 102
Blood pressure, 307, 310t
Blood urea nitrogen (BUN), 204, 210–211
Body surface area, nomogram for, 306, 307f
Bortezumab, 219
Botulinum toxin, 79, 99
Bowel bladder dysfunction (BBD), 70, 80
nocturnal enuresis and, 82
Bowel dysfunction and constipation, 52, 87–93, 313t
Bristol stool score/ chart, 88, 89f
Malone antegrade continence enema surgery in, 103, 104f
medications for treatment and prevention of, 90t
neurogenic bowel and, 92–93
in spina bifida and urologic function, 103–104
urinary incontinence (daytime) and, 72, 78
Bowel preparations, 305, 306t
Breastfeeding, 58
Bristol stool score/chart, 88, 89f
Bupivacaine (Marcaine), 297t

C

Calcineurin inhibitors, 219
Calcitonin gene-related peptide, undescended testes and, 22
Calcitriol, 210
Calcium-based stones, 189
Calcium channel blockers, chronic kidney disease (CKD) and, 210
Caliectasis, 119
Cancer. *See* Oncology
Cancer antigen 125 (CA-125), 273, 275
Cathartics, pediatric dosage of, 304t
Catheterizable stomas, 100–101, 101f
Catheterization, 54, 96, 97, 98–99, 100–101, 101f, 135, 151, 157

Caudal epidural, 246
Cecoureterocele, 126
Cefazolin (Ancef), 299t, 305t
Ceftriaxone (Rocephin), 299t
Central nervous system (CNS), 95
Cephalexin (Keflex), 64t, 108, 299t, 305t
Cephalosporins, hematuria as side effect of, 188
Cervicitis, 278, 279t
Cefixime, 305t
Chancroid, 280t, 281, 281t
Childhood urologic cancers, 291–292
Chlamydia trachomatis, 277, 278, 279t, 282
Chlorthalidone, 193
Chorionic gonadotropin (Pregnyl), 303–304t
Chromosomal microarray (CMA), 34
Chromosomal sex disorders, 29
Chronic kidney disease (CKD), 207–211, 208t, 305, 305t
Chronic transplant glomerulopathy, 217
Ciliopathies, 215
Cimetidine (Tagamet), 188, 303t, 305t
Ciprofloxacin (Cipro), 299t, 305t
Circumcision, 1–7
  advantages and disadvantages of, 1–2
  anesthesia in, 6
  complications of, 3–6, 5t
  contraindications to, 2
  foreskin and, normal development and care of, 2
  hydronephrosis and, 108
  methods used in, 3, 4f, 5f
  phimosis penile adhesions and paraphimosis *vs.*, 2–3
  postoperative care of, 7
Cisplatin-based chemotherapy, 292
Citrate therapy, 193
Clean intermittent catheterization (CIC), 58, 286
  in spina bifida and urologic function, 96, 97, 98–99
Clear cell sarcoma of the kidney (CCSK), 231
Cloaca, 151

associated anomalies, 151
background, 151
definitive repair of, 153
embryology, 151
initial management of cloacal malformation, 153
outcomes, 153
testing and diagnosis, 153
Cloacal exstrophy, 143, 145, 148
Cloacal malformation, 151
Cloacal membrane, 145
Coelomic epithelium, 29
Colace, 91. *See also* Docusate
Complete androgen insensitivity syndrome (CAIS), 39t, 49, 165–166
Complete gonadal dysgenesis (Swyer syndrome), 165
Complete primary repair of exstrophy (CPRE), 146, 147
Computed tomography (CT), 121, 130, 223
Computerized matching algorithms, 214
Conditioning treatment, for nocturnal enuresis, 85
Congenital adrenal hyperplasia (CAH), 24, 33, 35, 71, 74, 290
Congenital anomalies, 141–158
exstrophy-epispadias complex in, 143–144f, 143–148
imperforate anus in, 148–151, 149f
prenatal diagnosis and treatment in, 156
prognosis for, 157
prostate and posterior urethra in, 155
prune belly (Eagle-Barrett) syndrome, 60, 154–157, 155f
serum creatinine levels in, 156
sports recommendations for children with, 250
surgical intervention in, 157
testicles and scrotum in, 155, 157
treatment of, severe, moderate, mild, 156–157
urachal anomalies, 141, 142f, 143
ureters in, 154
urinary tract infection and, 52–53
urodynamic evaluation in, 157
voiding cystourethrogram (VCUG) in, 156
Congenital anomalies of the kidneys and urinary tract (CAKUT)

urinary tract infection and, 52–53
Congenital heart disease, hydronephrosis and, 121
Congenital megaureter, 111, 112f, 120f, 123–124
Congenital mesoblastic nephroma (CMN), 230–231
Congenitalism, 283, 284
Connective tissue disorders and hernias, 50
Constipation. *See* Bowel dysfunction and constipation
Continence, 285
Continuous antibiotic prophylaxis (CAP), 57, 63
Continuous incontinence and ectopic ureter, 271–272
Corticosteroids, immunosuppression in transplantation using, 217, 218, 219
Cosmesis, 285–286
Cotrimoxazole (Bactrim), 16
Cranberry products, 58
Creatinine clearance, 156, 306, 308f
Credé maneuver (suprapubic compression), 97
Cremasteric reflex, 19, 161
Cryptorchidism, 19–27
and cancer, 22
classification of, 19–20
definition of, 19
diagnosis of, 23–25
embryology of, 21
etiology of, 21–22
hormonal evaluation, 24–25
hormonal therapy, 25
imaging of, 23–24
incidence of, 20–21
physical examination, 23, 24f
prune belly (Eagle-Barrett) syndrome and, 155
sexual function and fertility, 22
surgery, 25–26
Cyclophosphamide, 226
Cyclosporin, 217–218, 219
Cyproheptadine, 210
Cystic/dysplastic kidneys. *See* Multicystic dysplastic kidney (MCDK)
Cystic partially differentiated nephroblastoma, 231

Cystinosis, 215
Cystinuria, nephrolithiasis and, 189, 190
Cystogram (nuclear medicine), vesicoureteral reflux and, 62–63
Cystoscopy, 78, 130, 169
Cystostomy, 153
Cysts, 141, 142f, 271

D

Daclizumab, immunosuppression in transplantation using, 218
Dactinomycin, 230
Database of pediatric urology, 295–313
Delayed puberty, 164–166. *See also* Abnormalities of sexual differentiation
  complete androgen insensitivity syndrome (CAIS), 165–166
  complete gonadal dysgenesis (Swyer syndrome), 165
  Kallmann syndrome, 165
  Klinefelter's syndrome, 165
  Turner syndrome, 165
Denys-Drash syndrome, Wilms tumor and, 227, 230
Dermoid cysts. *See* Mature cystic teratomas
17-20 Desmolase deficiency, 40t
Desmopressin acetate (DDAVP), 83–84, 302t
Detrusor-striated sphincter dysfunction (DSSD), 98
Dextranomer hyaluronic acid copolymer (Deflux), 65
Dialysis, chronic kidney disease (CKD) and, 211
Diet, 91, 192–193
Dihydrotestosterone (DHT), 22, 31
Dimercapto-succinic acid (DMSA), 62
Direct vision internal urethrotomy (DVIU), 289
Disorders of sex development (DSDS), 31–32, 33f
  evaluation, 32
  proposed nomenclature, 31
Disorders of sexual differentiation (DSD), 291
Distal vaginal atresia, 273
Diuretic renography, 121, 122f
  ectopic ureters and, 130
DMSA scan, 56, 62, 102, 156
Docusate (Colace), 304t

Donor sources for transplantation and, 213, 214–215
Donor-specific antibodies (DSA), 214
Donovanosis, 281
Doppler ultrasonography, 175
Doppler ultrasound, 161
Dorsal slit method circumcision, 3
Double hydrodistention implantation (double HIT) technique, 65
Down syndrome, anesthesia and, 244
Doxorubicin, Wilms tumor and, 230
Drug dosage recommendations in renal insufficiency, 305, 305t
Drug formulary, 295, 296–304t
Duodenal atresia, 148
Duplicated collecting syndrome anomaly, vesicoureteral reflux and, 60
Duplication, 148
Duplication anomalies, 273
Duplications, 109. *See also* Hydroureteronephrosis
Dye testing, ectopic ureters and, 130
Dyspareunia, 287

E

Eagle-Barrett syndrome. *See* Congenital anomalies,prune belly (Eagle-Barrett) syndrome
Ectopic testes, 19, 20f, 25
Ectopic ureters, 109, 127–130, 128–129f, 130, 150. *See also* Hydroureteronephrosis
  continuous incontinence and, 271–272
Eculizumab, 219
Ehlers-Danlos syndrome, hernias and, 50
Ejaculatory duct, 31
Electrolyte solution, 306t
Embolization techniques, 172
EMLA local anesthetic, 3, 6
Enalapril, 209
Encopresis, 88
End-stage renal disease (ESRD), 207, 213, 214, 290. *See also* Acute kidney injury (AKI);Chronic kidney disease (CKD)
Endocrine abnormalities, undescended testes and, 22

Endocrine function, 30–31
Endopyelotomy, hydronephrosis and, 116
Enemas, 91
Enterobacter, 51
Enterococcus, in urinary tract infection, 51
Epidermal growth factor, undescended testes and, 22
Epididymal inflammation, 161
Epididymis, 31
Epididymitis, 159, 159–162, 160t, 161f, 277–278, 279t, 285
Epidural anesthesia, 246
Epispadias, 143, 145, 146–147, 148. *See also* Exstrophy-epispadias complex
Epithelial tumors, 274–275
Epoophoron, 31
Epstein-Barr virus, transplantation and, 219, 220
Erectile dysfunction (ED), 286–287
Erythromycin, 306t
Escherichia coli, 51
Esophageal atresia, 151
  hydronephrosis and, 121
Estradiol, 34
Estrogen, 31
Everolimus, immunosuppression in transplantation using, 218
Exploration, 172
Exstrophy, 285–287
  continence, 285
  cosmesis, 285–286
  fertility, 286
  quality of life, 287
  sexual function, 286–287
  urinary tract infections (UTIs), 285
Exstrophy-epispadias complex, 143–144f, 143–148
Extracorporeal shock wave lithotripsy (ESWL), 196–197
Extravesical ureteroneocystostomy, 220

F

Face, legs, activity, cry, consolability (FLACC), 246
Femoral hernia. *See* Hernias, femoral

Fertility, exstrophy and, 286
Fertility and sexual function
oncologic treatment and, 230
in prune belly (Eagle-Barrett) syndrome, 157
in spina bifida, 104
undescended testes and, 19, 22
in varioceles, 163–164, 163f
Fetal hydronephrosis, vesicoureteral reflux and, 61
Fiber, constipation and, 91
Fluconazole (Diflucan), 301t, 305t
Flucytosine (5-FC), 301t, 305t
Fluid intake, 83, 91, 192, 204, 209, 295
Fluorescent treponemal antibody absorption (FTA-ABS), 278
Focused assessment with sonography for trauma (FAST) examination, 168
Follicle-stimulating hormone (FSH), 34, 165, 274
Formulary, 295, 296–304t
Formulas/calculations, 295–313
Fractionated or incomplete voiding, urinary incontinence (daytime) and, 76
Freehand surgical excision circumcision, 3, 5f
Furosemide, 187, 188, 204, 205, 209, 210

G

GAP procedure, in hypospadias, 11, 12f
Gartner duct cysts, 31, 271
Gender behavior, 34
Gender dysphoria, 34
General anesthesia (GA), 245
and developing brain, 245–246
Genetic disorders, 10, 81
Genital anomalies (female). *See* Gynecology, pediatric/adolescent, genital anomalies in
Genital herpes, 278
Genital ulcers, 278, 279–280t, 281–282
Genital warts. *See* Warts
Genitogram, 34
Genitourinary anomalies, 148
imperforate anus and, 150

Genitourinary trauma. *See* Trauma, genitourinary
Gentamicin, 299t, 305t
Germ cell tumors (GCT), 232, 274
Giggle incontinence, 71–72, 74
Glomerular basement disorders, 183–184, 201
Glomerular filtration rate (GFR), 207, 210, 306, 309f
Glomerulonephritis (GN), 180, 184–187, 201, 208
Goldenhaar syndrome, anesthesia and, 244
Gomco clamp circumcision, 3, 4f
Gonadal development, 29
Gonadal dysgenesis, mixed, 34, 36, 38t
Gonadal ridge, 29
Gonadal stroma tumors, 233
Gonadoblastomas, 233
Gonadotropin-releasing hormone (GnRH), 165
Gonococcal urethritis (GU), 277
Graft loss/rejection in transplantation, 219
Granuloma inguinale, 280t, 281, 281t
Granulomatosis (Wegener)/microscopic polyangiitis nodosa, 186–187
Granulosa cell tumors, 233
Growth and development, 138, 220
Gubernaculum testes, 21
Gynecology, pediatric/adolescent, 269–275. *See also* Adolescent urology;sexual abuse
  agenesis, 273
  anal examination in, 262, 263f
  examination positioning for, 259–261, 260f, 261f
  genital anomalies in, 271f
  hymenal variations in, 262–263
  injuries to, 174
  rhabdomyosarcoma and, 226, 227
  sexual abuse in, 174
  vesicovaginal voiding and, 71, 74, 80
Gynecology, pediatric and adolescent, 269
  intralabial anomalies, 269–272
  müllerian and vaginal anomalies, 272–273
  ovarian masses, 274–275

H

Haemophilus ducreyi, 281
Hematuria, 177–188
  causes of, 178t
  historical features and associated diseases, 179t
  laboratory evaluation, 183t
  physical findings and associated diseases, 180t
  treatment algorithm, 181–182f
Hemihyperplasia, 33
Hemitrigone, ectopic ureters and, 130
Hemolytic uremic syndrome (HUS), 201, 215, 244
Henoch-Schönlein purpura (systemic vasculitis), 186
Hermaphroditism, 36. *See also* Congenital adrenal hyperplasia
Hernia uterae inguinale, 50
Hernias, femoral, 45
Hernias, inguinal, 10–11, 45, 45–50, 47f, 145, 236
Hernias, strangulated, 45
Herpes (Herpes simplex), 265, 278, 279t, 281t
Herpes simplex virus-1 (HSV1), 278
Herpes simplex virus-2 (HSV2), 278
Hinman syndrome (nonneurogenic neurogenic bladder ; NNNB), 70, 80
Histamine blockers, pediatric dosage of, 303t
HIV infection, 265
HLA antigen system testing, in transplantation, 214–215
Hormonal disorders, 25–26, 82, 165. *See also* Abnormalities of sexual differentiation
Hormonal treatments, pediatric dosage of, 303–304t
Horseshoe kidney, 250
Human chorionic gonadotropin (hCG), 22, 25, 31
Hurler-Hunter syndrome, hernias and, 50
Hydralazine, 205
Hydroceles, 45–50, 46f
Hydrochlorothiazide, 193
Hydronephrosis, 53
Hydronephrosis (UPJ obstruction), 107–108, 111–118, 112f, 113f, 114t, 119, 120–123, 120f
  diuretic renography in, 121, 122f

ectopic ureters in, 127–130
fetal. *See* Fetal hydronephrosis,vesicoureteral reflux and
hematuria and, 188
imperforate anus and, 121, 150
radionuclide scanning in, 114–115, 121, 122f
schematic of, *versus* congenital megaureter, 111, 112f, 120f
sports recommendations for children with, 249
ureteroceles in, 124–127
Hydroureter, imperforate anus and, 150
Hydroureteronephrosis, 53, 119–130, 120f
17α-Hydroxylase deficiency, 40t
21α-Hydroxylase deficiency, 35
diagnosis, 35
treatment, 35–43
17-Hydroxyprogesterone (17-OHP), 33, 35
3β-Hydroxysteroid dehydrogenase deficiency, 31, 40t
17β-Hydroxysteroid dehydrogenase deficiency, 40t
Hyoscyamine (Levsin), 303t
Hyper bladder, 71, 74
Hyper or spastic bladder, 80
Hypercalciuria, 187–188, 189
Hyperkalemia, 33
acute kidney injury (AKI) and, 204
Hyperoxaluria, nephrolithiasis and, 189, 190
Hypertension, 117, 205, 209–210, 215, 220, 307, 310t
Hyperuricosuria, nephrolithiasis and, 189, 190
Hypnosis, for nocturnal enuresis, 85
Hypocalcemia, acute kidney injury (AKI) and, 204
Hypocitraturia, nephrolithiasis and, 189, 190
Hypogonadotropic hypogonadism, 165
Hyponatremia, 33
Hypoplastic/dysplastic kidney disease, transplantation and, 214
Hypospadias, 9–17, 287–289
anomalies associated with, 10–11
classification of, 9, 10f
embryology of, 9
follow-up care of, 17

incidence, genetics and etiology of, 10
meatal advancement and glanuloplasty procedure (MAGPI) in, 11, 13f
Onlay island flap procedure in, 11, 14f
postoperative symptoms and care of, 14–17
primary tubularizations in, 11, 12f, 13f
salvage repairs in, buccal mucosa harvested for, 12, 15f
straightening of penis in, 12, 16f
surgical techniques for, 11–12
urinary diversion drippy stent for, 16f
Hypospadias Objective Scoring Evaluation and Pediatric Penile Perception Score, 288
Hypothalamus, 165

I

Ibuprofen (Motrin, Advil), 16, 297t
Ideal body weight, 306
IgA nephropathy, 185–186
Ilioinguinal blocks, 247
Imipramine hydrochloride, 84–85
Imipramine (Tofranil), 302t
Immunosuppressive therapy in transplantation, 214, 217–219
Imperforate anus, 121, 148–151, 149f
Imperforate hymen, 269
presenting as a vaginal bulge with cyclic abdominal pain during puberty, 270f
In vitro fertilization (IVF), 287
Incontinence. *See* Urinary incontinence
Inguinal hernia. *See* Hernias, inguinal
Inhibin, 273
undescended testes and, 22
Interleukin-2 inhibitors/blockers, immunosuppression in transplantation using, 217–218
International Society of Pediatric Oncology (SIOP), Wilms tumor recommendations, 230
Intralabial anomalies, 269–272
imperforate hymen and, 269
Intratubular germ cell neoplasia (IGCN), 232

Intravenous fluid therapy guidelines, 295
Intravenous pyelography (IVP), 169
Introital cysts, 271
Ipsilateral salpingo-oophorectomy, 274

J

Juvenile granulosa cell tumors (JGCT), 274

K

Kallmann syndrome, 165
Kayexelate. *See* Sodium polystyrene sulfonate
Ketorolac (Toradol), 297t
Kidney stones. *See* Urolithiasis
Kidneys and renal function. *See* Acute kidney injury (AKI);Chronic kidney disease (CKD)
King procedure, hypospadias and, 11
Klebsiella, urinary tract infection and, 51
Klebsiella granulomatis, 281
Klinefelter syndrome, 165

L

Labetalol, 205
Labial adhesions/anomalies, 269
Laboratory findings, calculations/formulas for. *See* Formulas/calculations
Lactate dehydrogenase (LDH), 273
Lactulose (Enulose), 90t, 91
Laparoscopic techniques, 197
Laparoscopy, 24, 49, 130, 235–239, 329
Latex allergy and precautions, in spina bifida, 104–105
Laxatives, 89
Lazy bladder, 71, 74, 80
Leukemia, priapism and, 175
Leydig cell tumors, 233
Leydig cells, 30
  differentiation, sexual differentiation abnormalities and, 30
  hypoplasia, 39t
  testosterone production from, 31

Li-Fraumeni syndrome, rhabdomyosarcoma and, 225
Lidocaine, 6, 297t
Living related donors (LRD) for transplantation and, 213, 214
Lower pole heminephrectomy, 272
Lubricants, for constipation, 90
Lumbar/thoracic epidural, 247
Luteinizing hormone (LH), 22, 25, 31, 34, 165, 274
Luteinizing hormone releasing hormone (LHRH) treatment, undescended testes and, 25
Lymphogranuloma venereum, 280t, 281t, 282

M

MAG 3 Lasix Renogram, 121, 122f. *See also* Radionuclide scanning
Magnesium citrate (Milk of Magnesia), 89, 90t, 306t
Magnetic resonance imaging (MRI), 105, 130, 223, 273
Magnetic resonance urograms, 121, 272
Male sex-specific germ cells, 30
Malone antegrade continence enema surgery, 93, 103, 104f
Malrotation, 148
Mature cystic teratomas, 274
Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, 273
Meatal advancement and glanuloplasty procedure (MAGPI), 11, 13f
Meckel's diverticulum, 148
Medical expulsive therapy (MET), 192
Megaureter. *See* Congenital megaureter
Megestrol acetate, 210
Membranoproliferative glomerulonephritis (MPGN), 185, 186
Men who have sex with men (MSM), 282
Meningomyelocele, chronic kidney disease (CKD) and, 208
Mesenchymal dysplasia syndrome. *See* Prune belly (Eagle-Barrett) syndrome
Mesonephric duct (wolffian), 29, 31
Metabolic acidosis, 33
  urethral valves (posterior) and, 138
Metabolic diseases, 189, 189–190, 215
Metaiodobenzylguanidine (MIBG) scans, 223–224
Methylphenidate, 79
Metronidazole (Flagyl), 299t

Microscopic polyangiitis nodosa, 186–187
Micturition difficulties, 153
Midazolam, 245
Mineral oil, 90, 90t, 304t
Mirabegron, 79
Mixed gonadal dysgenesis, 34, 36, 38t
Modern staged repair of exstrophy (MSRE), 146
Mogen clamp circumcision, 3
Monoclonal antibodies, as T cell antibody therapy in transplantation, 218
Morphine sulfate, 297t
Müllerian and vaginal anomalies, 272–273
Müllerian ducts, sexual differentiation abnormalities and, 29, 30f, 31
Müllerian inhibiting substance (MIS), sexual differentiation abnormalities and, 31, 34
Multicystic dysplastic kidney (MCDK), 108, 116–118, 117f, 121, 150, 249
Multidisciplinary treatment groups, development of, 284
MYCN oncogene, amplification of, 223, 225
Mycophenolate mofetil, immunosuppression in transplantation using, 218, 219
Myelodysplasia, 109
Myelomeningocele. *See* Spina bifida/neurogenic bladder

N

Narcotics, 247
Neisseria gonorrhoeae, 277, 278, 279t
Neomycin, 306t
Nephrectomy, 172
  and nephroureterectomy, 238, 249
Nephroblastoma, cystic partially differentiated, 231
Nephrogenic adenoma, 233–234
Nephrolithiasis, 187–188, 189–193, 192t
Nephroma, congenital mesoblastic (CMN), 230–231
Neural blockade, 246
Neuroblastoma. *See* Oncology,neuroblastoma in
Neurofibromatosis, 225
Neurogenic bladder, 53, 60, 150
  management of, 290

Neurogenic bowel, 92–93
Newborns, diagnosis and treatment of common disorders in, 35
  21α-hydroxylase deficiency, 33, 35–43
  mixed gonadal dysgenesis (MGD), 36
  overtesticular DSD, 36
  46,XY DSD, 36
Nitrofurantoin, 56–57, 64t, 300t, 305t
Nocturnal enuresis (bed wetting), 72, 81–85
Nongonococcal urethritis (NGU), 277
Nonneurogenic neurogenic bladder (NNNB; Hinman syndrome), 70, 80
Nonsteroidal anti-inflammatory drugs (NSAIDs), 188, 247
North American Pediatric Renal Transplant Cooperative Study (NAPRTCS), 213
NPO guidelines for anesthesia, 244
Nuclear medicine cystogram, 62–63
Nuclear medicine renal scan, 62
Nucleic acid amplification tests (NAATs), 277
Nutrition and growth in presence of chronic kidney disease (CKD), 210

O

Obstructed hemivagina unilateral renal anomalies syndrome (OHVIRA) syndrome, 273
  with ipsilateral atrophic and dysplastic kidney, 272f
Obstruction, hydroureteronephrosis and, 119
Obstructive uropathy, transplantation and, 214
Ocean Spray Cranberry Classic, 58
OKT3 monoclonal antibodies, as T cell antibody therapy in transplantation, 218
Oncology, 223–234
  angiomyolipoma (AML) in, 231
  bladder tumors in, 233–234
  clear cell sarcoma of the kidney (CCSK) in, 231
  congenital mesoblastic nephroma (CMN) in, 230–231
  cystic partially differentiated nephroblastoma in, 231
  fertility and, 256
  gonadal stroma tumors in, 233
  gonadoblastomas in, 233

Leydig, Sertoli, granulosa cell tumors in, 233
neuroblastoma in, 223–225
renal cell carcinoma (RCC) in, 231
rhabdoid tumor of the kidney (RTK) in, 231
rhabdomyosarcoma, 225–227
teratoma in, 232, 233
testicular tumors in, 50, 232–233
undescended testes and, 22
Wilms tumor in, 117, 227, 227–230
yolk sac tumor in, 233
Ondansetron (Zofran), 301t
Onlay island flap procedure, hypospadias and, 11, 14f
Online pediatric urology recommendations, 315–316
Open surgery, 197
Osteodystrophy, renal, 210
Ovarian development, 31
Ovarian follicles, 31
Ovarian masses, 274–275
epithelial tumors, 274–275
germ cell tumors, 274
sex cord–stromal tumors, 274
Overactive bladder (OAB). *See* Uninhibited bladder (unstable, overactive or spastic bladder)
Overtesticular DSD, 43
Oxybutynin (Ditropan), 16, 79, 84, 303t

P

Pain control in children, Wong-Baker faces pain scale, 242f
Pampiniform venous plexus, varioceles, 163–164, 163f
Paramesonephric duct (müllerian), 29, 31
Paraphimosis, 2–3
Paraurethral cysts, 271
Paroophoron, 31
Partial androgen insensitivity, 39t
Patient-controlled analgesia (PCA), 247
Pediatric urologic oncology. *See* Oncology
Pelvic floor dysfunction (PFD), 70

Pelviectasis, 119
Pelvocaliectasis, 119
Penicillin, 188
Penile blocks, 247
Penis. *See also* Circumcision;Hypospadias
  length of, 33t, 307, 309f
  phimosis penile adhesions and paraphimosis in, 2–3, 52
  priapism and, 175
  straightening of, 12
  traumatic injury to, 174
Penopubic epispadias, 148
Percutaneous calculi extraction, 199f
Percutaneous nephrolithotomy (PCNL), 195, 197
Peristeen Anal Irrigation System, 93
Periurethral injection therapy, in spina bifida, 101
Persistent cloaca, 151
Persistent müllerian duct syndrome, 39t
pH level of urine, nephrolithiasis and, 189
Phenazopyridine (Pyridium), 302t
Phenytoin, hematuria as side effect of, 188
Phimosis penile adhesions and paraphimosis *vs.*, 2–3, 52
Physical development parameters, 310, 311t
Physicians' Desk Reference (PDR), 248
Pierre Robin syndrome, anesthesia and, 244
Plastibell clamp circumcision, 3
Polyangiitis nodosa, microscopic, 186–187
Polyethylene glycol (Miralax), 89, 90t, 91, 304t, 306t
Polymerase chain reaction (PCR), 281
Polyuria, 82, 137
Posterior sagittal anorectoplasty (PSARP), 150
Posterior urethral valves. *See* Urethral valves (posterior)
Posttransplant lymphoproliferative disorders (PTLD), 217
Potassium citrate, 193
Preformed reactive antibodies (PRA) testing in transplantation, 214
Pregnyl. *See* Chorionic gonadotropin
Prenatal urologic diagnosis and maternal counseling, 107–110
  duplications, ectopic ureters, ureteroceles in, 109

findings of urologic examination and, 107
general treatment guidelines and, 107
hydronephrosis and, 107–108, 121
imperforate anus and, 150
in utero interventions and, 107
incidence of urologic anomalies and, 107
multicystic dysplastic kidney in, 108
myelodysplasia and, 109
prune belly (Eagle-Barrett) syndrome and, 156
urethral valves (posterior) and, 108, 131–133
urethral valves in, 108
urinary tract obstruction and, 109
Prerenal azotemia, acute kidney injury (AKI) and, 201
Priapism, 175
Primary hyperoxaluria, 215
Primordial germ cells (PGCs), 29, 31
Probiotics, 58
Prochlorperazine (Compazine), 301t
Prolapsed mucosa, surgical excision of, 271
Prolapsed ureterocele, 271
Propantheline (Pro-Banthine), 303t
Prostate
prune belly (Eagle-Barrett) syndrome and, 155
rhabdomyosarcoma and, 226, 227
Protease inhibitors, hematuria as side effect of, 188
Proteinuria, 180, 188
Proteus, urinary tract infection and, 51
Prune belly (Eagle-Barrett) syndrome. *See* Congenital anomalies,prune belly (Eagle-Barrett) syndrome
Pseudoephedrine (Sudafed), 303t
Pseudomonas aeruginosa, 51
Psychological stress and enuresis, 72, 82
Puberty, delay of. *See* Delayed puberty
Pyelocaliectasis, 119
Pyelonephritis, 57, 61, 122, 124, 201
Pyeloplasty, 116, 236, 237f, 238
Pyramid procedure, hypospadias and, 11

R

Radiocontrast imaging, in chronic kidney disease (CKD), 210–211
Radioisotope clearance, 114–115
Radionuclide scanning, 114–115, 116, 121, 122f
Ranitidine (Zantac), 303t, 305t
Rapamycin, 219
Rapid plasma reagin (RPR) test, 278
Recommendations, online pediatric urology recommendations, 315–316
Reflux, resolution of, 63
Reflux nephropathy, 53, 59, 214. *See also* Vesicoureteral reflux
Regional anesthesia, 246
Rejection in transplantation, 219
Renal agenesis, 150, 249
Renal and bladder ultrasound (RBUS), 55–56, 60, 62
Renal cell carcinoma (RCC), 231
Renal ectopia, imperforate anus and, 150
Renal exploration, 172
Renal injury grading system (grades 1 to 5), 169
Renal insufficiency, urethral valves (posterior) and, 137–138. *See also* Acute kidney injury (AKI);Chronic kidney disease (CKD)
Renal osteodystrophy, 138, 210
Renal salvage, 172
Renal transplantation. *See* Transplantation
Renal ultrasounds, 228
Reoperative hypospadias, 289
Rhabdoid tumor of the kidney (RTK), 231
Rhabdomyosarcoma. *See* Oncology,rhabdomyosarcoma
Rituximab, 219
Robotics, 235–239
Rokitansky nodule, 274

S

Salt-losing nephropathy, urethral valves (posterior) and, 137–138
Saran wrap, 146
Scrotal ultrasound, 277
Self-reporting, 246
Seminal vesicle, 31

Seminiferous tubules, 30
Senna (Ex Lax; Ducolax; Senokot), 90–91, 90t, 304t
Sertoli cell tumors, 233
Sertoli cells, 30, 31
Sertoli-Leydig cell tumors, 274
Sevelamer, 210
Sex chromosomes, 29
Sex cord–stromal tumors, 274
Sex determining factor (SRY), 29, 31, 34
Sex differentiation, 29
Sex of rearing, 34–35
Sexual abuse, 257–267. *See also* Gynecology, pediatric/adolescent
  accidental injury *vs.*, differentiation of, 265, 266t
  acute assault and rape kit use in, 267
  anal examination in, 262, 263f
  definition of, 257
  documentation of findings in, 262
  examination (hymenal) techniques used in, 261–262
  examination positioning for, 259–261, 260f, 261f
  findings of examination in, 262–263, 264t
  history taking in, 258
  HIV infection and, 265
  management of, doctors legal responsibility in, 265–266
  medical indicators of possible, 258, 258t
  physical examination for, 259–266
  physical findings of, 263–264, 266t
  presentation of, 258
  risk factors for, 257
  sexually transmitted diseases and, 265
  vaginal injury and, 174
Sexual differentiation, abnormalities of. *See* Abnormalities of sexual differentiation
Sexual function. *See* Fertility and sexual function
Sexual health, 288–299, 289
Sexually transmitted diseases, 265, 277
  cervicitis, 278
  diagnosis and management of, 279–280t

epididymitis, 277–278
genital ulcers, 278, 281–282
urethritis, 277
Sexually transmitted infections (STIs), 161
Shield technique circumcision, 3
Shimada classification, neuroblastoma, 224
Shock wave lithotripsy, 195–197
Short-gut syndrome, 148
Sickle-cell disease, 175, 188
Single-site (port) surgery, 236
Sirolimus, immunosuppression in transplantation using, 218
Sleep disorders, nocturnal enuresis and, 82
Snodgrass procedure, hypospadias and, 11, 13f
Sodium excretion fraction, in acute kidney injury (AKI), 202–203
Sodium polystyrene sulfonate (Kayexelate), 204
Soft tissue reconstruction, 146
Sonograms, 76
Spastic bladder, 71, 74, 80, 98
Spermatic vein, varioceles, 163–164, 163f
Spina bifida, 289–290
Spina bifida/neurogenic bladder, 95–106
anticholinergics in treatment of, 98
artificial urinary sphincter for, 102, 103f
bacteriuria and, 102
bladder function improvement in, 98–101
bladder neck suspension and reconstruction in, 102
bowel management and, 103–104
catheterizable stomas and, 100–101, 101f
classification of, 95, 96t
clean intermittent catheterization (CIC) in treatment of, 96, 97, 98–99
continence (sphincter function) evaluation in, 101–102
Credé maneuver (suprapubic compression) in treatment of, 97
delivery, method of birth and, 96
diagnosis of, 96–97
DMSA scan in, 102
latex allergy and precautions in, 104–105
long-term management of, 98–105

Malone antegrade continence enema surgery in, 103, 104f
medications for, 99
myelomeningocele and, 105–106
neurologic injury and disease, 98
newborn assessment and care of, 96–97
periurethral injection therapy in, 101
prenatal assessment for, 96
renal function and, 102
serum alpha-fetoprotein (AFP) levels and, 96
sexual function and fertility in, 104
spinal dysraphism and, 95, 96t, 105
surgical bladder augmentation in, 99–101, 100f
surgical intervention in, 96
treatment of, in newborn, 97–98
ultrasound assessment in, 96, 97
urinalysis and culture in, 97
urinary tract infection and, 102
urodynamic evaluation of, in planning treatment of, 97
urologic goals in treatment of, 95
vesicoureteral reflux and, 102
Spinal anomalies, 78
Spinal dysraphism, 95, 96t, 105
Spinal narcotic anesthesia, 246
Sports recommendations for children with genitourinary abnormalities, 249–255
Staccato (intermittent stream) voiding, urinary incontinence (daytime) and, 75–76
Stent placement, 169
Steroidogenic acute regulatory protein deficiency, 40t
Stimulant type laxatives, 90–91
Stool softeners, 91
Sulfamethoxazole, 305t
Surveillance imaging, 193
Sympatholytics, pediatric dosage of, 303t
Sympathomimetics, pediatric dosage of, 303t
Syphilis, 278, 280t, 281, 281t
Systemic agents, 247

Systemic lupus erythematosus (SLE), 185, 186, 208
Systemic vasculitis, 186–187

T

T cell antibody therapy in transplantation, 218–219
Tacrolimus, immunosuppression in transplantation using, 217–218, 219
Tamsulosin (Flomax), 303t
Tanner stages, 164, 310, 312f. *See also* Delayed puberty
Teratoma, 232, 233
Testicles and scrotum
  ascending testes, 21
  cremasteric reflex and, 19
  feminization of, 49
  hernias and. *See* Hernias, inguinal
  hydroceles and, 45–50. *See also* Hydroceles
  laparoscopy and, surgical repair of, 236
  masses in, 50
  prune belly (Eagle-Barrett) syndrome and, 155, 157
  rhabdomyosarcoma and, 226
  sports recommendations for children, following injury to, 250, 254–255
  testicular torsion in, 50, 159–162, 160t, 161f
  traumatic injury to, 174
  tumors of, 50, 232–233. *See also* Oncology, testicular tumors in
  undescended testes in, 10–11, 19–26, 20f, 50, 250
  vanishing testes syndrome and, 24
  varicoceles in, 163–164
Testicular cords, 30
Testicular torsion. *See* Testicles and scrotum,testicular torsion in
Testis hypotrophy, 164
Testosterone, 22, 25, 31, 34
Testosterone production, 31
Thiazide diuretics, 193
  hematuria as side effect of, 188
Thiersch-Duplay procedure, hypospadias and, 11
Thymoglobulin. *See* Antithymocyte globulin
Timed voiding therapy, 78, 83, 137
Tobramycin (Tobrex), 300t, 305t

TP53 (tumor protein 53) gene mutations, 227
Tracheoesophageal fistula, 151
Transabdominal ultrasound, 274
Transient wetting, 71, 80
Transitional cell carcinoma, 234
Transitional urology, 283
  challenges, 283–284
  children with childhood cancers, 291–292
  conditions, 284–285
  disorders of sexual differentiation (DSD), 291
  exstrophy, 285–287
  hypospadias, 287–289
  implications for the future, 292
  posterior urethral valves (PUV), 290–291
  research, 284
  spina bifida, 289–290
  timing of transition, 285
Transplantation, 213–222
  antibiotic prophylaxis following, 220
  antigen system testing in, ABH and HLA systems in, 214–215
  chronic kidney disease (CKD) and, 211
  complications of, 220
  donor sources for, 213, 214–215
  end-stage renal disease (ESRD) and, 213, 214
  etiology and demographics of, 214
  graft loss/rejection in, 219
  growth and development following, 220
  hypertension following, 220
  hypoplastic/dysplastic kidney disease and, 214
  immunosuppressive therapy in, 214, 217–219
  infection following, 220
  living related donors (LRD) for, 213, 214
  North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) in, 213
  obstructive uropathy and, 214
  preformed reactive antibodies (PRA) testing in, 214
  pretransplant recipient preparation in, 215–217

reflux nephropathy and, 214
Transverse vaginal septum, 273
Trauma, genitourinary, 167–175, 168f, 173f. *See also* Sexual abuse
sexual abuse *vs.*, 265, 265t
sports-related injury in, 252–253
Treponema pallidum, 278
Treponema pallidum particle agglutination (TP-PA) assay, 278
Trichomoniasis vaginalis, 278, 279t
Tricyclic antidepressants, 79
Trimethobenzamide (Tigan), 302t
Trimethoprim-sulfamethoxazole (Septra; TMP-SMX), 56, 57, 64t, 300t
Trimethoprim (TMP), 300t, 305t
Tumors. *See* Oncology
Turner syndrome, 29, 38t, 165

U

Ultrasonography, 168
Undescended testicles and scrotum. *See* Testicles and scrotum,undescended testes in
Uninhibited bladder (unstable, overactive or spastic bladder), 71, 74, 80, 87
UPJ obstruction. *See* Hydronephrosis
Upper airway obstruction, nocturnal enuresis and, 82
Upper pole heminephrectomy, 272
Urachal anomalies. *See* Congenital anomalies,urachal anomalies
Urachal diverticulum, urachal anomalies and, 142, 142f
Urachal sinus, urachal anomalies and, 141, 142f
Urachus, 141, 142f
Ureteral ectopy. *See* Ectopic ureters
Ureteral reimplantation using laparoscopy, 239
Ureterectasis, 119
Ureteroceles, 109, 119, 124–127, 126–127, 126f. *See also* Hydroureteronephrosis
Ureteropelvic junction (UPJ) injuries, 172
Ureteropyelography, 169
Ureteroscopic calculi extraction, 198f
Ureteroscopy, in urolithiasis, 195, 197
Ureteroureterostomy, 130, 220

Ureterovesical junction obstruction, hydroureteronephrosis and, 119
Ureters, 109, 111, 112f, 120f, 123–124, 172–173, 173f
  prune belly (Eagle-Barrett) syndrome and, 154
Urethra, 162–163, 173–174, 269, 271f
  prune belly (Eagle-Barrett) syndrome and, 155
Urethral prolapse, 269–271
Urethral valves (posterior), 108, 131–139, 132f, 133f, 134f, 290–291
Urethritis, 277, 279t
Urethrorrhagia, 162–163
Urinalysis, 55, 74, 83, 97, 202, 209
Urinary diversion, 146
Urinary incontinence (daytime), 69–80
  age of continence and, social parameters for, 69
  algorithm for, 77f
  alpha blockers in treating, 79
  antibiotic prophylaxis and, 79
  anticholinergics for treatment of, 79
  associated problems with, 72
  bacteriuria/urinary tract infection and, 72
  behavior modification treatment for, 78
  benign urinary frequency and, 70, 74, 80
  biofeedback training and, 80
  bladder control and, development of, 69
  bowel bladder dysfunction and, 70, 80
  bowel dysfunction and, 72, 78
  classification of, 70–72
  constipation and, 78, 87
  cystoscopy in, 78
  definition of incontinence in, 69
  diagnosis of, 72–78
  epidemiology of, 72
  exstrophy-epispadias complex and, 147
  fractionated or incomplete voiding in, 76
  giggle incontinence and, 71–72, 74
  lazy bladder in, 71, 74, 80
  medication for, 78–79
  methylphenidate in treating, 79

nocturnal enuresis (bed wetting) and, 72. *See also* Nocturnal enuresis
nonneurogenic neurogenic bladder (NNNB; Hinman syndrome), 70, 80
oxybutynin in treating, 79
pelvic floor dysfunction (PFD) in, 70
physical examination in, 74
psychological stressors and, 72
sonogram/ultrasound for, 76
sphincter activity and, 70, 70f
spinal radiograph in, 78
spontaneous cure rate of, 72
staccato (intermittent stream) voiding and, 75–76
surgical treatment in, 80
symptoms of (potty dance; Vincent's curtsy; holding), 72, 73f
timed voiding treatment for, 78
transient wetting and, 71, 80
treatment of, 78–80
tricyclic antidepressants in treating, 79
uninhibited bladder (unstable, overactive or spastic bladder) in, 71, 87
urinalysis in, 74
urinary flow rate measurement in, 75–76
vesicoureteral reflux and, 72
vesicovaginal voiding and, 71, 74, 80
video urodynamic study in, 77–78
voiding cystourethrogram (VCUG) in, 77
voiding diary for, 74–75, 75–76f
voiding dysfunction and, 70, 70f, 72, 73f, 74
voiding frequency disorders in, 71, 80
x-ray imaging of bladder in, 77
Urinary tract infections, 51–58, 177
antibiotics for, treatment and prophylaxis,–57
asymptomatic bacteriuria in, 55
bacteria implicated in, 51
bladder abnormalities and, 52
bladder and bowel dysfunction, 52
catheterization and, 54
chronic kidney disease (CKD) and, 208
congenital anomalies of the kidneys and urinary tract and, 52–53

congenital megaureter and, 124
constipation/encopresis and, 87
diagnosis of, 55, 56f
DMSA scan in, 56
epidemiology of, 51
female anatomic factors for, 52
gender ratio of, by age, 51, 52t
genetics, 54
hematuria and, 187. *See also* Hematuria
imaging studies for, 55–56
male anatomic factors for, 52
nephrolithiasis and, 191
neurogenic bladder and, 53
nocturnal enuresis and, 82
phimosis and, 52
presentation and symptoms of, 54–55
prevention of, 57–58
prior UTI, 52
reflux nephropathy and, 53
renal papillary configuration and, 53, 54f
risk factors for, 51–54
special circumstances for, 58
in spina bifida, 102
treatment of, 56–58
ultrasound imaging in, 55–56
urinalysis in, 55
urinary incontinence (daytime) and, 72
urine collection and culture for, 55
urologic instrumentation, 54
vesicoureteral reflux in, 53, 53f, 59–67. *See also* vesicoureteral reflux
voiding cystourethrogram (VCUG) in, 56
Urinary tract infections (UTIs), 285
Urinary tract obstruction, prenatal diagnosis of, and maternal counseling for, 109
Urine culture, 55, 83, 97
Urine output and voiding habits, 310, 312t, 313t
Urodynamic evaluation, 62, 83, 96, 97, 150, 157

Urogenital mobilization, 153
Urolithiasis, 196f. *See also* Extracorporeal shock wave lithotripsy (ESWL)
Urologic anomalies. *See* Prenatal urologic diagnosis and maternal counseling
Urologic Instrumentation, 54
Urologic oncology. *See* Oncology
Utricle or Mullerian remnant, hypospadias and, 10–11

V

VACTERL association, 151
VACTERL syndrome, 121, 150, 244
Vagina. *See under* Gynecology, pediatric/adolescent
Vaginal agenesis, 273
Vaginal atresia, 273
Vaginoplasty, 35
Vaginostomy tube, 153
Valsalva void, 285
Valve bladder syndrome, urethral valves (posterior) and, 133, 136
Valves unilateral reflux and renal dysplasia (VURD) syndrome, 135
Vanishing testes syndrome, 24
Varicoceles, 163–164, 163f
Vas deferens, 31
Vascular thrombosis, transplantation and, 219
Vasculitis, chronic kidney disease (CKD) and, 208
Vasculitis, systemic, 186–187
VATER syndrome, 244
Venereal Disease Research Laboratory (VDRL) test, 278
Vesicostomy, 153
  urethral valves (posterior) and, 135–136
Vesicoureteral reflux, 59–67, 145
  chronic kidney disease (CKD) and, 208
  constipation and, 87
  grading of, 61, 61t, 62f
  imperforate anus and, 150
  in spina bifida and urologic function, 102
  surgical correction of, 64–66, 65f, 66f, 138
  urethral valves (posterior) and, 135, 138
  urinary incontinence (daytime) and, 72

urinary tract infection and, 53, 53f, 59, 61
Vesicovaginal voiding, 71, 74, 80
Videourodynamic study, urinary incontinence (daytime) and, 77–78
Vincent's curtsy (holding), 73f
Vincristine, 230
Virilized external genitalia, 35
Vital signs, 307, 310t
Vitamin D, renal osteodystrophy, 210
Voclosporin, 219
Voiding cystoureterogram (VCUG), 56, 59, 62, 77, 114, 116, 121, 124, 127, 130, 135, 146, 156, 162
Voiding diary, 74–75, 75f
instructions, 76f
Voiding dysfunction, 70, 70f, 72, 73f, 74, 133
Voiding frequency disorders, 80

W

WAGR syndrome, Wilms tumor and, 227
Warts, 265
Web sites of interest, 315–316
Wegener granulomatosis/microscopic polyangiitis nodosa, 186–187
Wilms tumor. *See* OncologyWilms tumor in
"Withholding" phenomenon, constipation and, 87–88
Wolffian ducts, sexual differentiation abnormalities and, 30f, 31
Wong-Baker faces pain scale, 246f

X

X chromosome, 29
X chromosomes, sexual differentiation abnormalities and, 29
X-ray, 77, 83, 89
46,XX gonadal and ductal development, 31
46,XY DSD, 43
46,XY gonadal and ductal development, 30–31
46,XY pure gonadal dysgenesis (Swyer syndrome), 39t

Y

Y chromosome, 29

sexual differentiation abnormalities and, 29
Yolk sac tumor, 233